In the following claims, the subscript and superscripts of a given variable are distinct. For example, R_1 is distinct from R^1.

1.   An HIV protease inhibitor compound comprising a phosphonate group.

2.   An HIV protease inhibitor compound of claim 1 selected from:

a Saquinavir-like phosphonate protease inhibitor compound,

a Lopinavir-like phosphonate protease inhibitor compound,

a Ritonavir-like phosphonate protease inhibitor compound,

a Indinavir-like phosphonate protease inhibitor compound,

a Atazanavir-like phosphonate protease inhibitor compound,

a Nelfinavir-like phosphonate protease inhibitor compound,

a Tipranavir-like phosphonate protease inhibitor compound,

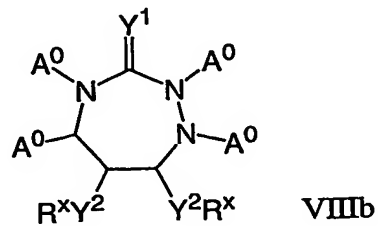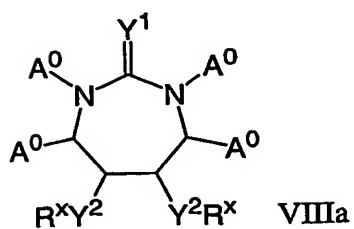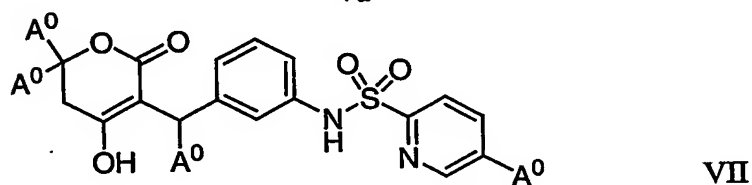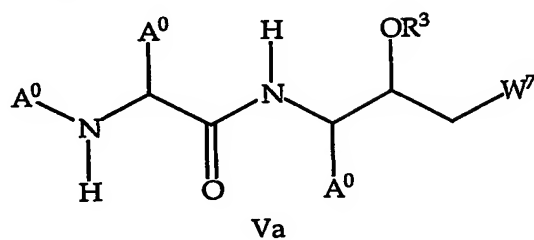a Amprenavir-like phosphonate protease inhibitor compound,

a KNI-like phosphonate protease inhibitor compound, and

a Cyclic Carbonyl-like phosphonate protease inhibitor compound;

and pharmaceutically acceptable salts, hydrates, and formulations thereof.

3.   A compound selected from the Formulas:

I

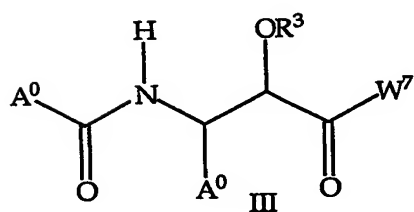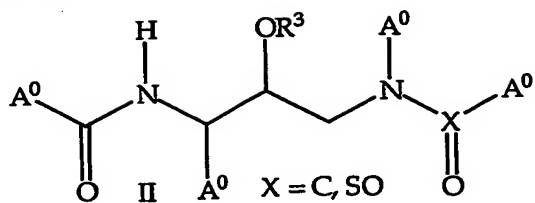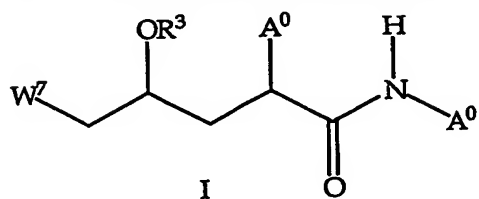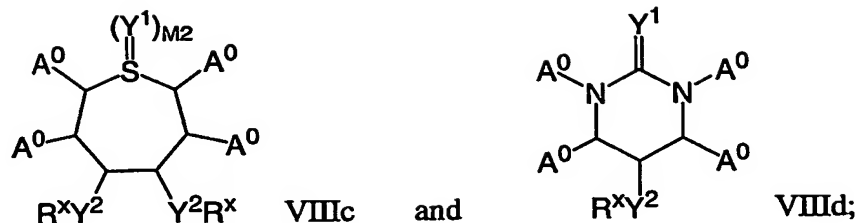II   X = C, SO

III

IV

V

VI

Va

VII

VIIIa

VIIIb

VIIIc   and   VIIId;

wherein:

A⁰ is A¹, A² or W³ with the proviso that the compound includes at least one A¹;

A¹ is:

;

A² is:

;

A³ is:

;

Y^1 is independently O, S, $N(R^x)$, $N(O)(R^x)$, $N(OR^x)$, $N(O)(OR^x)$, or $N(N(R^x)(R^x))$;

Y^2 is independently a bond, O, $N(R^x)$, $N(O)(R^x)$, $N(OR^x)$, $N(O)(OR^x)$, $N(N(R^x)(R^x))$, -$S(O)_{M2}$-, or -$S(O)_{M2}$-$S(O)_{M2}$-;

R^x is independently H, R^1, W^3, a protecting group, or the formula:

$$\left[\begin{array}{c} Y^1 \\ \bigvee \\ \cdot \end{array} Y^2 \right]_{M1a} \left[\begin{array}{c} R^y \quad R^y \\ \bigvee \end{array} (Y^2)\right]_{M12c} \left[\begin{array}{c} Y^1 \\ \bigvee \\ \end{array} Y^2 \right]_{M1c} \left[\begin{array}{c} \end{array}\right]_{M1d} R^y$$
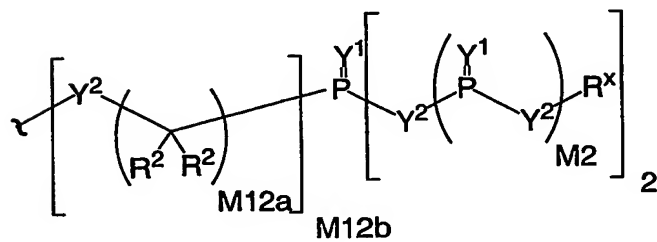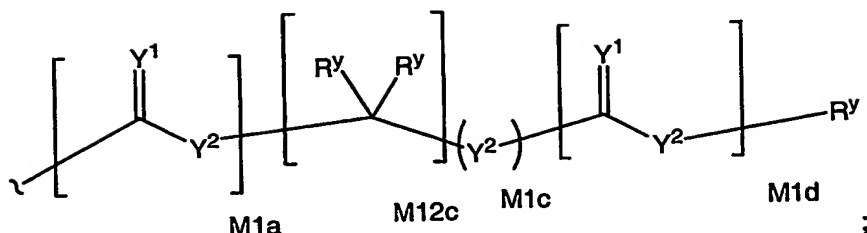
R^y is independently H, W^3, R^2 or a protecting group;

R^1 is independently H or an alkyl of 1 to 18 carbon atoms;

R^2 is independently H, R^1, R^3 or R^4 wherein each R^4 is independently substituted with

0 to 3 R^3 groups, or taken together at a carbon atom, two R^2 groups form a ring of 3 to 8

carbons and the ring may be substituted with 0 to 3 R^3 groups;

R^3 is R^{3a}, R^{3b}, R^{3c} or R^{3d}, provided that when R^3 is bound to a heteroatom, then R^3 is

R^{3c} or R^{3d};

R^{3a} is F, Cl, Br, I, -CN, N_3 or -NO_2;

R^{3b} is Y^1;

R^{3c} is -R^x, -$N(R^x)(R^x)$, -SR^x, -$S(O)R^x$, -$S(O)_2R^x$, -$S(O)(OR^x)$, -$S(O)_2(OR^x)$,

-$OC(Y^1)R^x$, -$OC(Y^1)OR^x$, -$OC(Y^1)(N(R^x)(R^x))$, -$SC(Y^1)R^x$, -$SC(Y^1)OR^x$,

-$SC(Y^1)(N(R^x)(R^x))$, -$N(R^x)C(Y^1)R^x$, -$N(R^x)C(Y^1)OR^x$, or -$N(R^x)C(Y^1)(N(R^x)(R^x))$;

R^{3d} is -$C(Y^1)R^x$, -$C(Y^1)OR^x$ or -$C(Y^1)(N(R^x)(R^x))$;

R^4 is an alkyl of 1 to 18 carbon atoms, alkenyl of 2 to 18 carbon atoms, or alkynyl of

2 to 18 carbon atoms;

R^5 is R^4 wherein each R^4 is substituted with 0 to 3 R^3 groups;

W^3 is W^4 or W^5;

W^4 is R^5, -$C(Y^1)R^5$, -$C(Y^1)W^5$, -SO_2R^5, or -SO_2W^5;

W^5 is carbocycle or heterocycle wherein W^5 is independently substituted with 0 to 3

R^2 groups;

W^6 is W^3 independently substituted with 1, 2, or 3 A^3 groups;

W^7 is a heterocycle bonded through a nitrogen atom of said heterocycle and

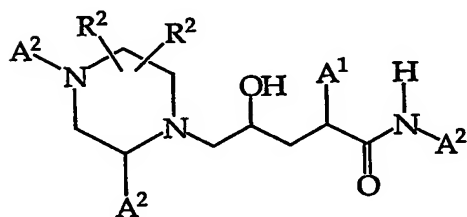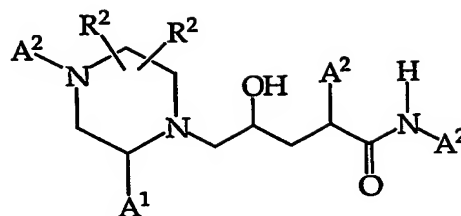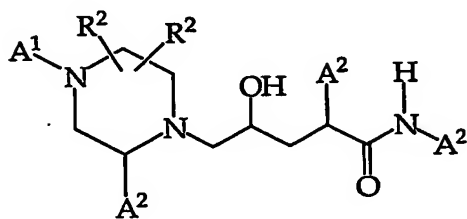independently substituted with 0, 1 or 2 A^0 groups;

M2 is 0, 1 or 2;

M12a is 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11 or 12;

M12b is 0, 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11 or 12;

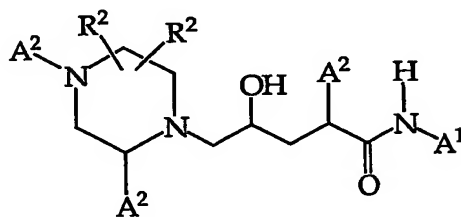M1a, M1c, and M1d are independently 0 or 1; and

M12c is 0, 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11 or 12.

4.   A compound of claim 3 selected from:

, and

5

5. A compound of claim 3 selected from:

6. A compound of claim 3 selected from:

, and

7.   A compound of claim 3 selected from:

,

,

and

.

8.   A compound of claim 3 selected from:

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,

,

and

9.   A compound of claim 3 selected from:

,

,

and

and

and

5

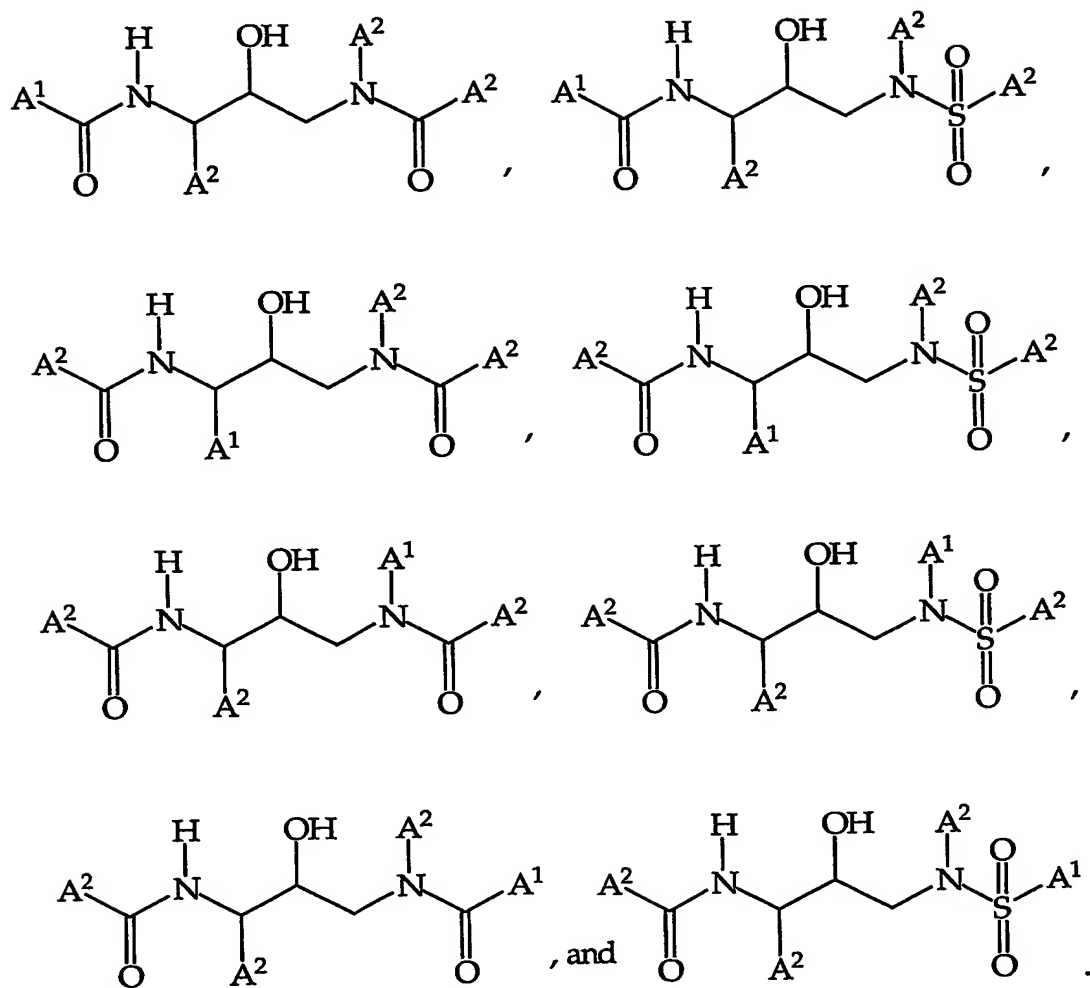10.   A compound of claim 3 selected from:
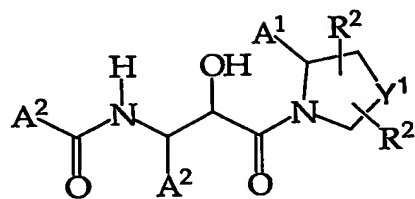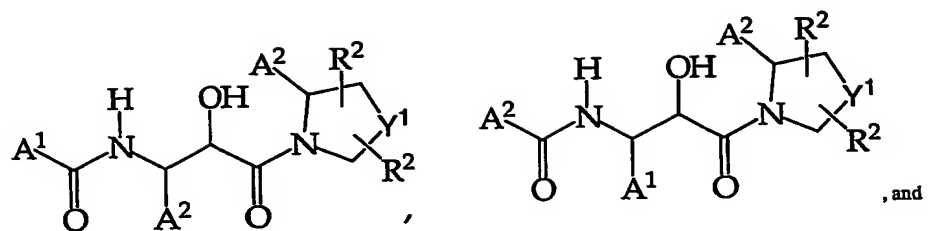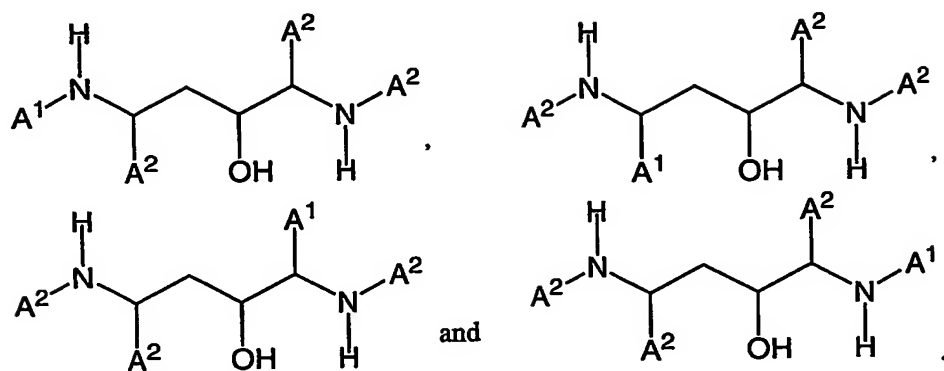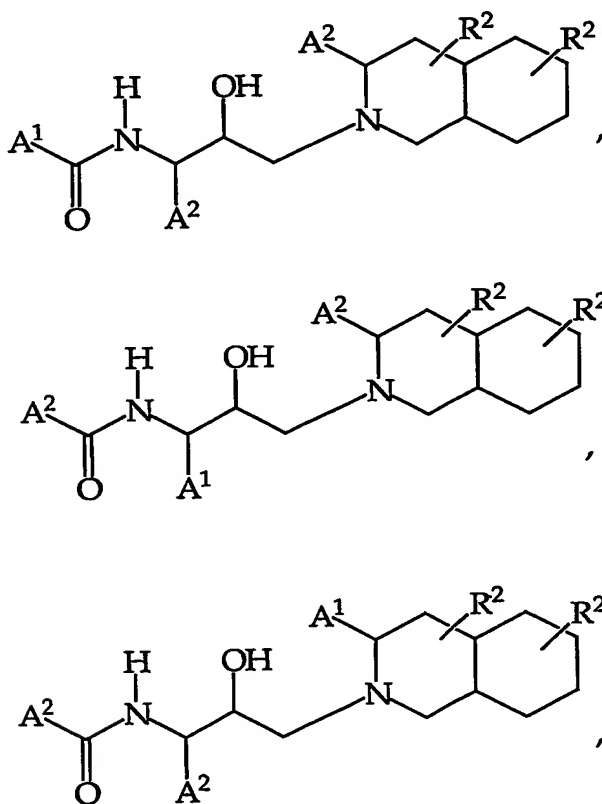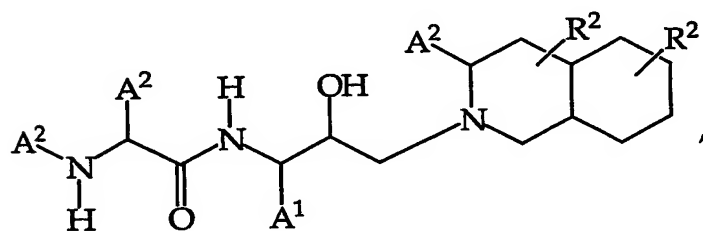

and

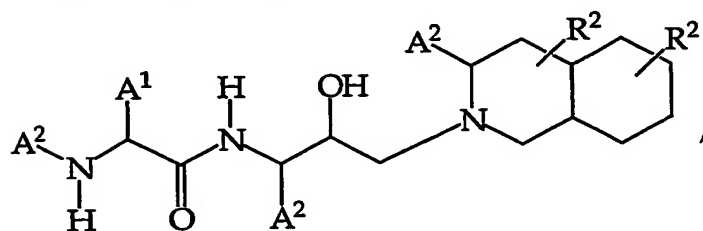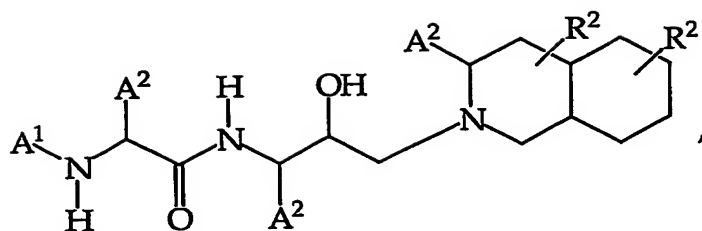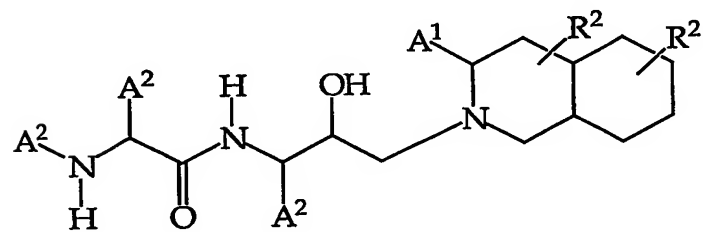11.   A compound of claim 3 selected from:
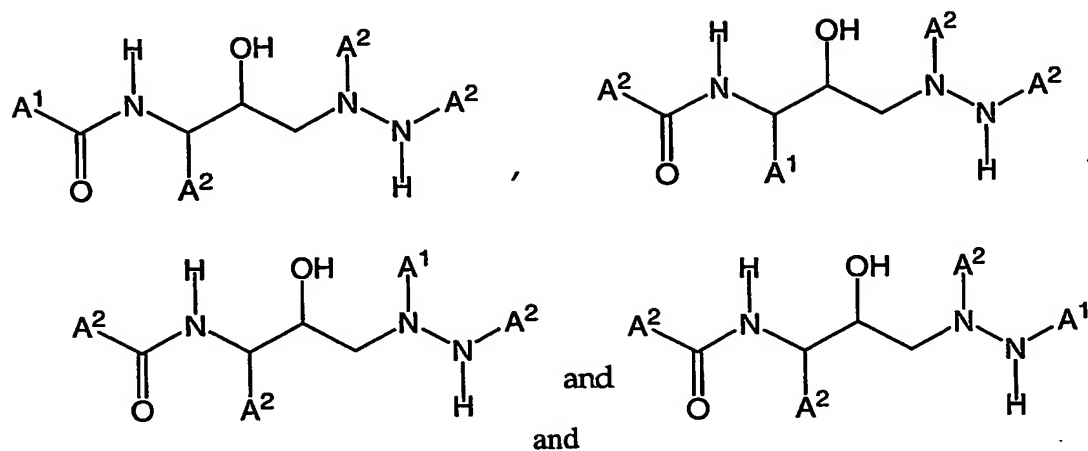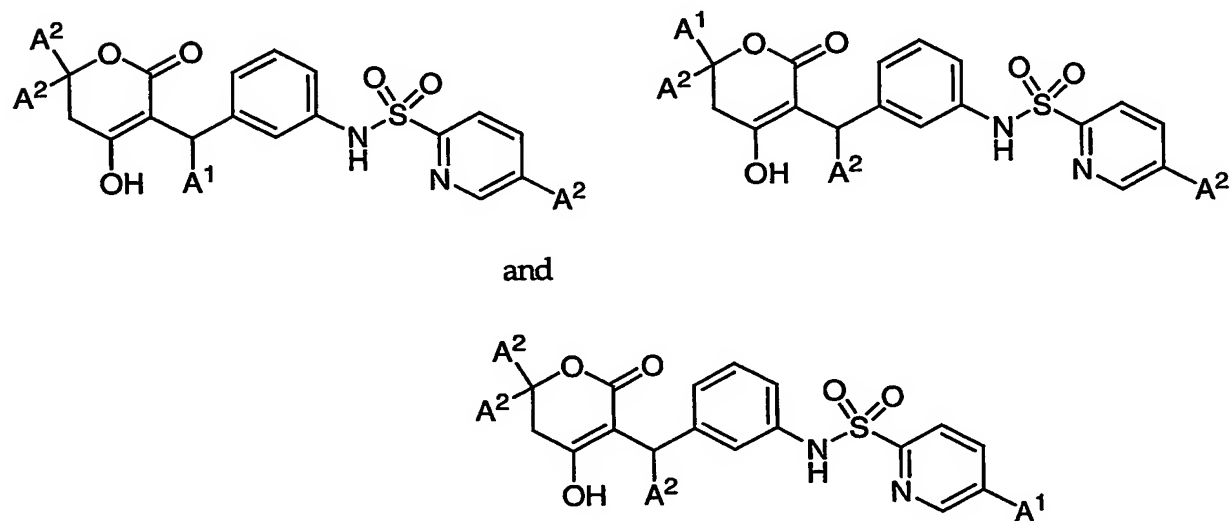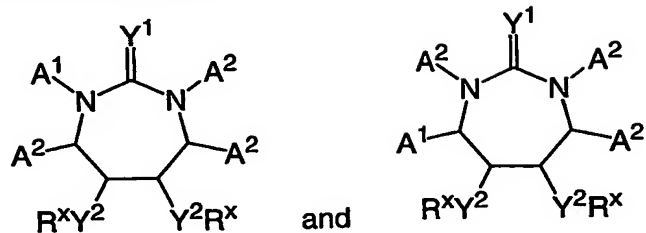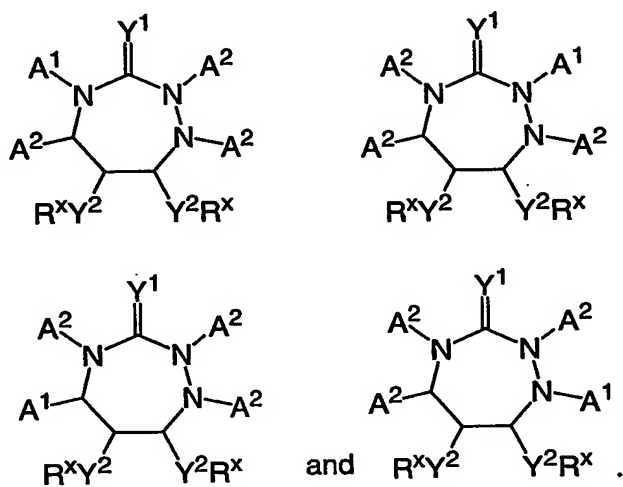

and

12.   A compound of claim 3 selected from:

and

13.   A compound of claim 3 selected from:

$$\text{structures}$$

and

14.   A compound of claim 3 selected from:

$$\text{structures}$$

and

15.   A compound of claim 3 wherein A^1 is of the formula:

$$\text{structure}$$
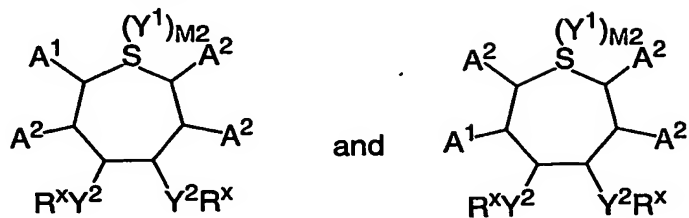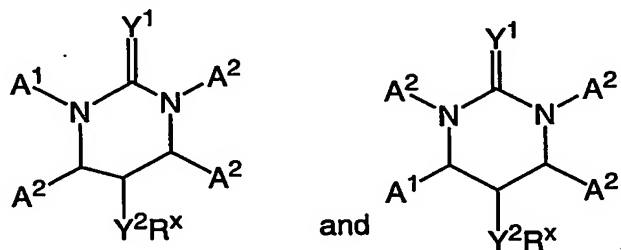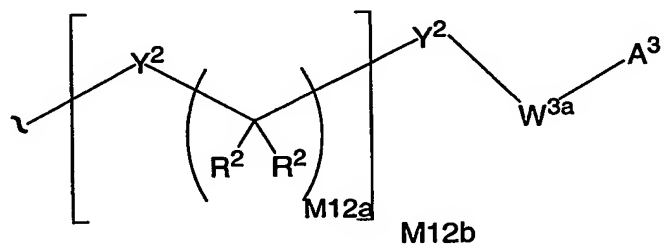
16.   A compound of claim 15 wherein A^1 is of the formula:

$$\left[^{Y^2}\left(_{R^2R^2}\right)_{M12a}^{W^{3a}}A^3\right]_{M12b}$$
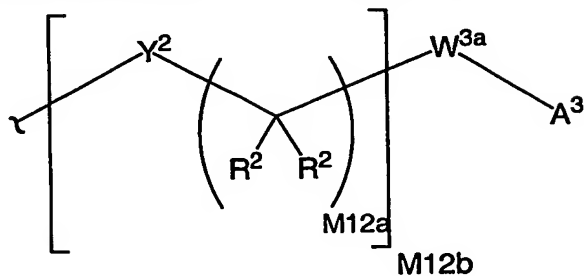
17.   A compound of claim 16 wherein A^1 is of the formula:

$$\left(_{R^2R^2}\right)_{M12a}^{W^{3a}}A^3$$
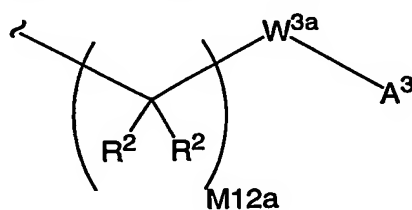
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18.   A compound of claim 17 wherein A^1 is of the formula:

$$\left(_{R^2R^2}\right)_{M12a}^{W^{5a}}A^3\quad;$$
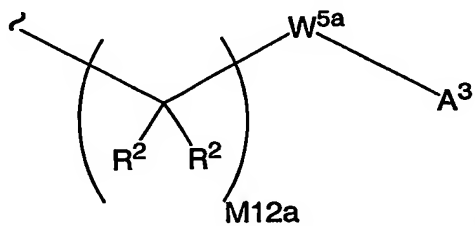
10   and W^{5a} is a carbocycle or a heterocycle where W^{5a} is independently substituted with

0 or 1 R^2 groups.

19.   A compound of claim 18 wherein M12a is 1.

-1659-

20.   A compound of claim 3 wherein A^3 is of the formula:

$$\left[\left[\underset{\underset{(\underset{M12a}{R^2\ R^2})}{}}{Y^2} \right] \overset{\overset{Y^1}{\parallel}}{P} \left[Y^2 R^x \right] \right]_2$$

M12b   .
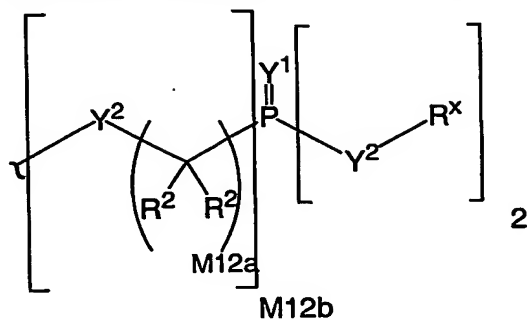
21.   A compound of claim 20 wherein A^3 is of the formula:

$$Y^2 \underset{\underset{M12a}{(R^2\ R^2)}}{} \overset{\overset{Y^1}{\parallel}}{P} \left[Y^2 R^x \right]_2$$

M12a   .
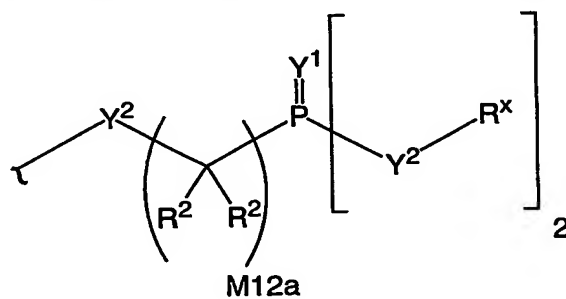
22.   The compound of claim 21 wherein A^3 is of the formula:

$$Y^{2a} \underset{\underset{M12a}{(R^2\ R^2)}}{} \overset{\overset{Y^{1a}}{\parallel}}{P} \left[Y^{2a} R^x \right]_2$$

M12a   ;
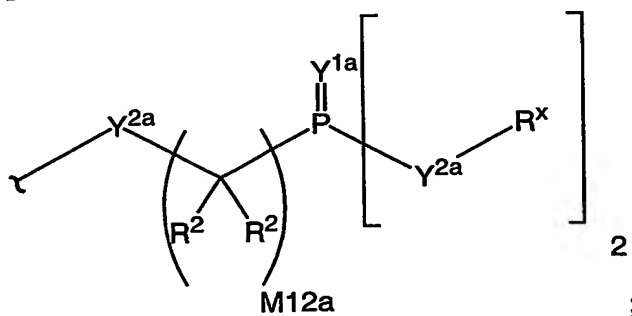
Y^{1a} is O or S; and

Y^{2a} is O, $N(R^x)$ or S.

23.   The compound of claim 22 wherein A³ is of the formula:

and Y²ᵇ is O or N(Rˣ).

24.   The compound of claim 23 wherein A³ is of the formula:

25.   The compound of claim 23 wherein A³ is of the formula:

R¹ is independently H or alkyl of 1 to 18 carbon atoms;

Y²ᵇ is O or N(Rˣ); and

M12d is 1, 2, 3, 4, 5, 6, 7 or 8.

26.   The compound of claim 25 wherein A^3 is of the formula:
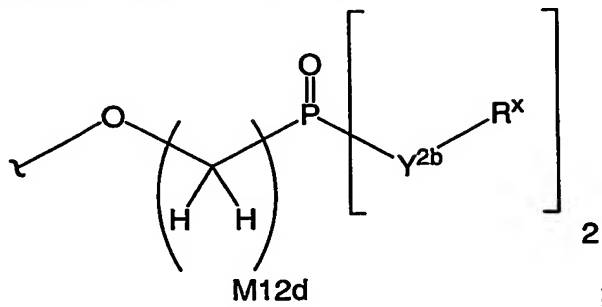
Y^{2b} is O or N(R^x); and

M12d is 1, 2, 3, 4, 5, 6, 7 or 8.

5

27.   The compound of claim 26 wherein M12d is 1.

28.   The compound of claim 3 wherein A^3 is of the formula:

29.   The compound of claim 28 wherein A^3 is of the formula:
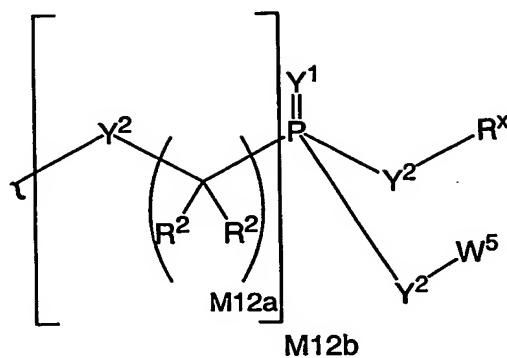
5   30.   The compound of claim 29 wherein W^5 is a carbocycle.

31.   The compound of claim 30 wherein A^3 is of the formula:
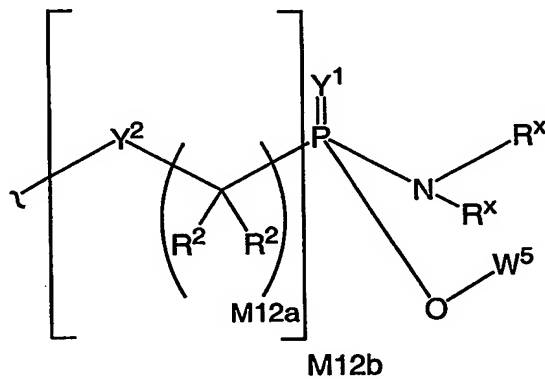
10   32.   The compound of claim 31 wherein W^5 is phenyl.

33.   The compound of claim 28 wherein M12b is 1.

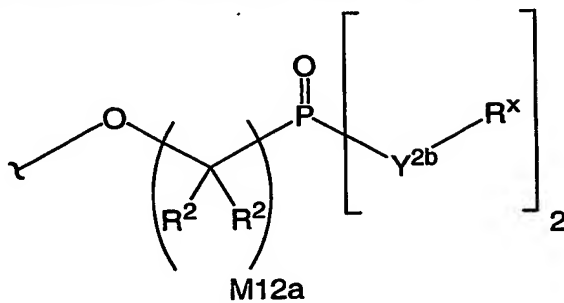34.   The compound of claim 33 wherein A^3 is of the formula:
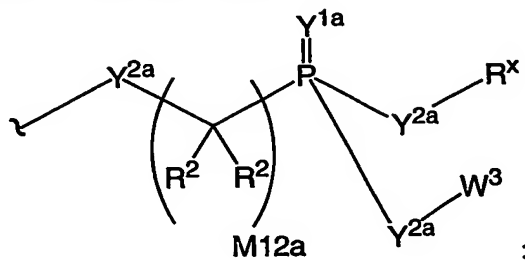
Y^{1a} is O or S; and
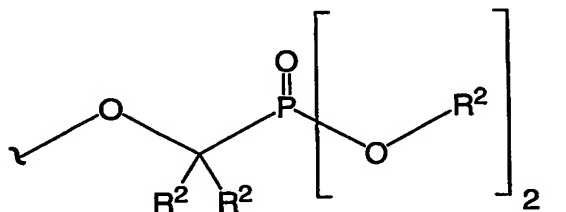
Y^{2a} is O, $N(R^x)$ or S.

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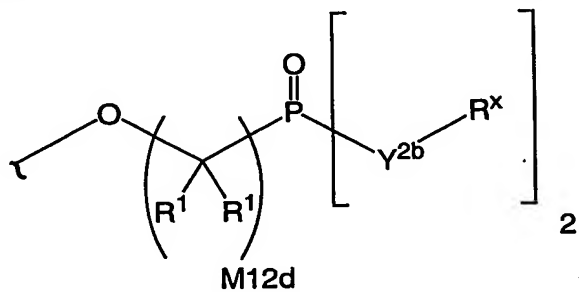35.   The compound of claim 34 wherein A^3 is of the formula:
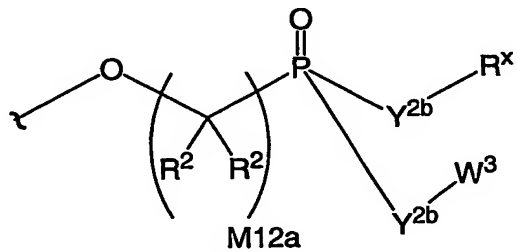
and Y^{2b} is O or $N(R^x)$.

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36.   The compound of claim 35 wherein A^3 is of the formula:

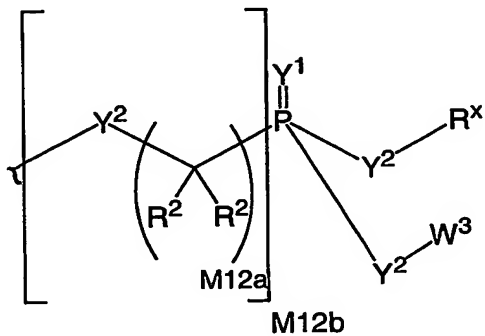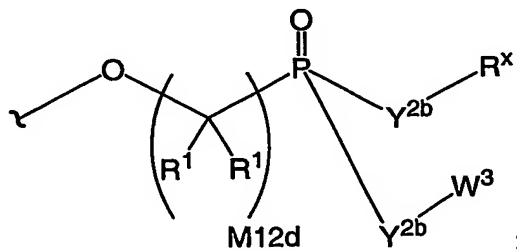R^1 is independently H or alkyl of 1 to 18 carbon atoms;

Y^{2b} is O or $N(R^x)$; and

M12d is 1, 2, 3, 4, 5, 6, 7 or 8.

15

37.   The compound of claim 36 wherein R^1 is H.

38.   The compound of claim 36 wherein M12d is 1.

39.   The compound of claim 36 wherein A^3 is of the formula:
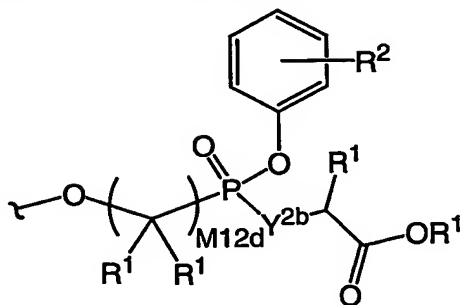
wherein the phenyl carbocycle is substituted with 0 to 3 R^2 groups.

5   40.   The compound of claim 39 wherein A^3 is of the formula:
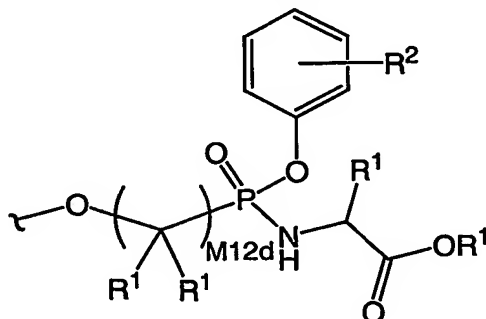
41.   The compound of claim 40 wherein A^3 is of the formula:
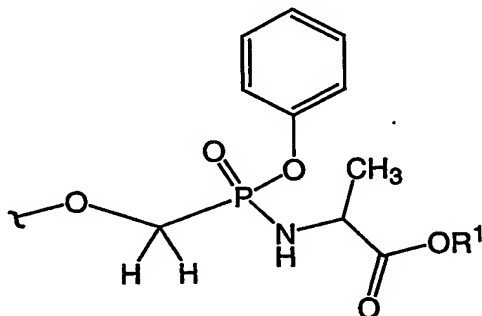
42.   A compound of claim 3 wherein R^x is of the formula:
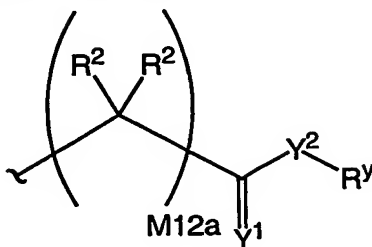
43.   A compound of claim 42 wherein R^x is of the formula:
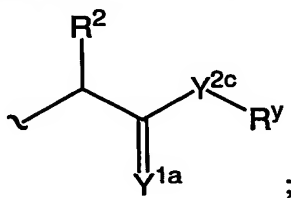
Y^{1a} is O or S; and

Y^{2c} is O, $N(R^y)$ or S.

44.   A compound of claim 43 wherein R^x is of the formula:
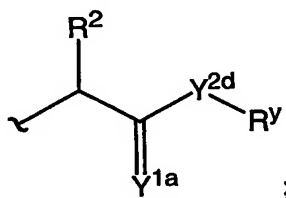
Y^{1a} is O or S; and

Y^{2d} is O or $N(R^y)$.

45.   A compound of claim 44 wherein R^x is of the formula:
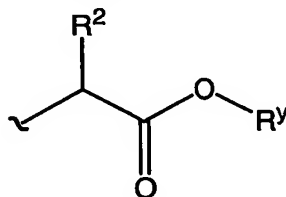
46.   A compound of claim 45 wherein R^x is of the formula:
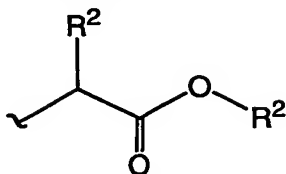
47.   The compound of claim 3 wherein R^x is of the formula:
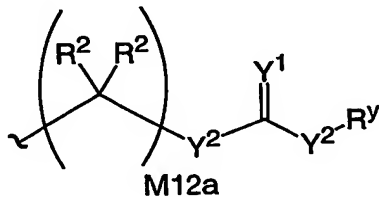
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48.   The compound of claim 47 wherein A^3 is of the formula:

10   49.   The compound of claim 3 wherein A^3 is of the formula:

; and

R^x is of the formula:

50.　　The compound of claim 49 wherein A^3 is of the formula:
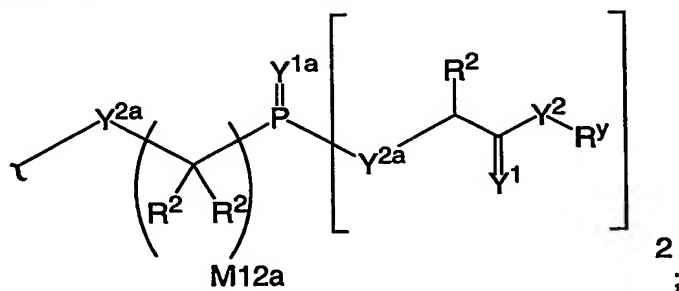
Y^{1a} is O or S; and

Y^{2a} is O, $N(R^2)$ or S.

51.　　The compound of claim 50 wherein A^3 is of the formula:
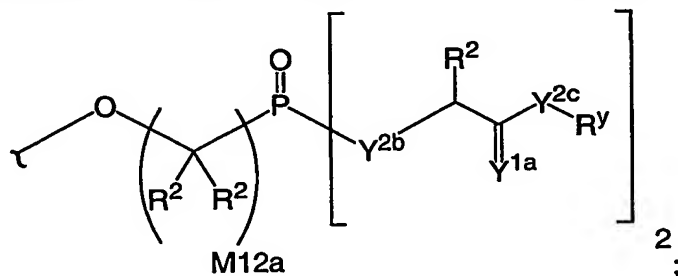
Y^{1a} is O or S;

Y^{2b} is O or $N(R^2)$; and

Y^{2c} is O, $N(R^y)$ or S.

52.　　The compound of claim 51 wherein A^3 is of the formula:

Y^{1a} is O or S;

Y^{2b} is O or $N(R^2)$;

Y^{2d} is O or $N(R^y)$; and

M12d is 1, 2, 3, 4, 5, 6, 7 or 8.

53.   The compound of claim 52 wherein A^3 is of the formula:

5

Y^{2b} is O or $N(R^2)$; and

M12d is 1, 2, 3, 4, 5, 6, 7 or 8.

54.   The compound of claim 53 wherein A^3 is of the formula:
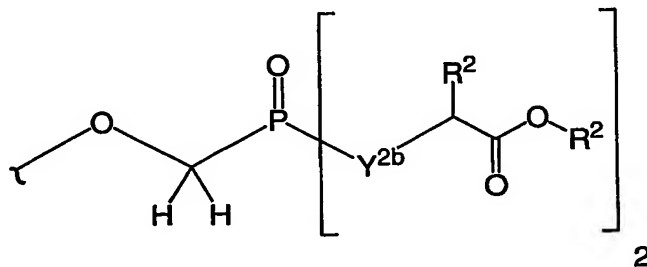
10

and Y^{2b} is O or $N(R^2)$.

55.   The compound of claim 54 wherein A^3 is of the formula:
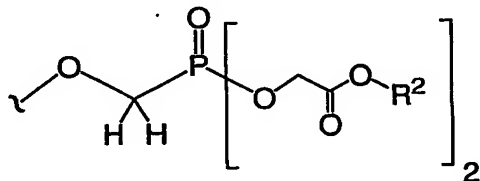
56.   The compound of claim 3 wherein A^3 is of the formula:

R^x is of the formula:

57.   The compound of claim 56 wherein A^3 is of the formula:
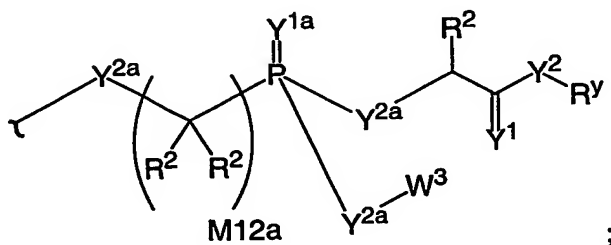
Y^{1a} is O or S; and

Y^{2a} is O, $N(R^2)$ or S.

58.   The compound of claim 57 wherein A^3 is of the formula:
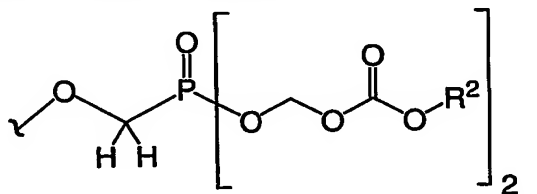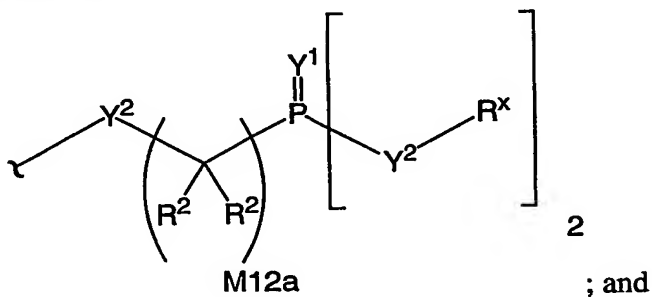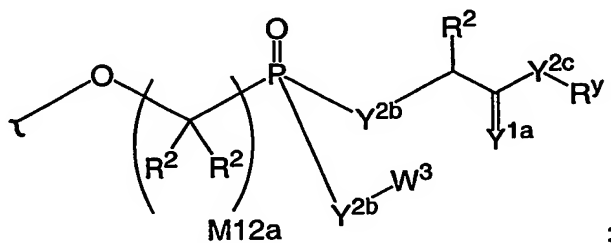

Y^{1a} is O or S;

Y^{2b} is O or $N(R^2)$; and

Y^{2c} is O, N(R^y) or S.

59.   The compound of claim 58 wherein A^3 is of the formula:
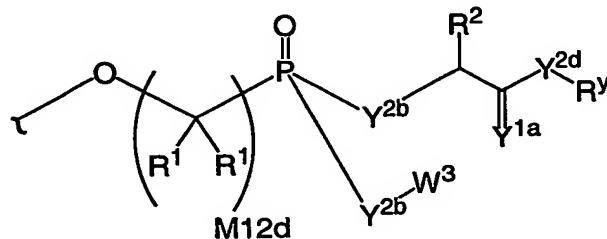
R^1 is independently H or alkyl of 1 to 18 carbon atoms;

Y^{1a} is O or S;

Y^{2b} is O or N(R^2);

Y^{2d} is O or N(R^y); and

M12d is 1, 2, 3, 4, 5, 6, 7 or 8.

60.   The compound of claim 59 wherein A^3 is of the formula:

;

Y^{2b} is O or N(R^2); and

M12d is 1, 2, 3, 4, 5, 6, 7 or 8.

61. The compound of claim 60 wherein A^3 is of the formula:

and Y^{2b} is O or N(R^2).

62.   The compound of claim 3 wherein A^1 is of the formula:

$$\left[Y^2 - \left(\overset{R^2}{\underset{R^2}{\text{C}}} \right)_{M12a} Y^2 - W^6 - A^3 \right]_{M12b} \quad ; \text{and}$$

A^3 is of the formula:

$$\left[Y^2 - \left(\overset{R^2}{\underset{R^2}{\text{C}}} \right)_{M12a} \overset{\overset{Y^1}{\|}}{\underset{}{P}} \left[Y^2 - R^x \right]_2 \right]_{M12b} \quad .$$

63.   The compound of claim 62 wherein A^1 is of the formula:

$$\left[Y^2 - \left(\overset{R^2}{\underset{R^2}{\text{C}}} \right)_{M12a} W^6 - A^3 \right]_{M12b} \quad ;$$

A^3 is of the formula:

$$\left[Y^2 - \left(\overset{R^2}{\underset{R^2}{\text{C}}} \right)_{M12a} \overset{\overset{Y^1}{\|}}{\underset{}{P}} \left[Y^2 - R^x \right]_2 \right] \quad ; \text{and}$$
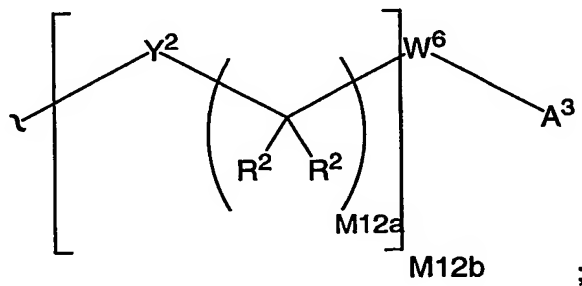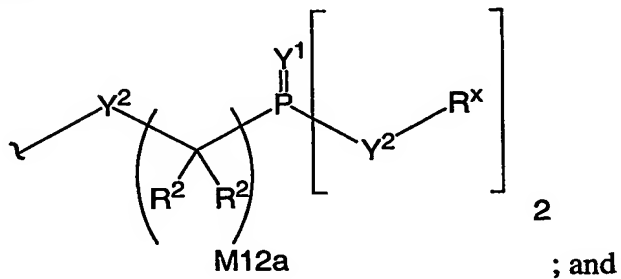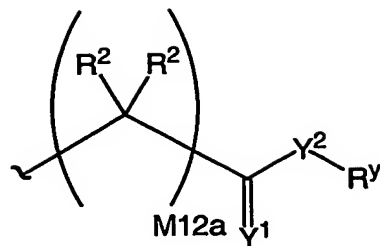
R^x is of the formula:

64.   The compound of claim 63 wherein A^1 is of the formula:
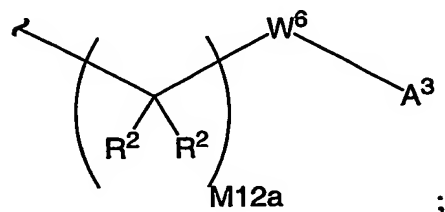
A^3 is of the formula:

Y^{1a} is O or S; and

Y^{2a} is O, $N(R^2)$ or S.

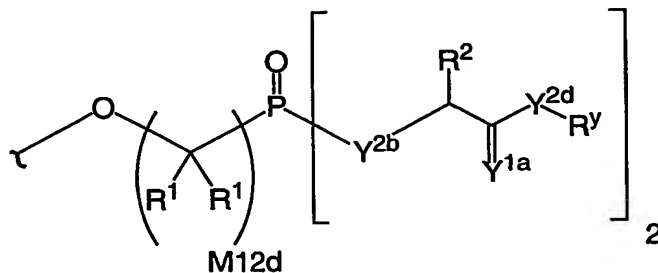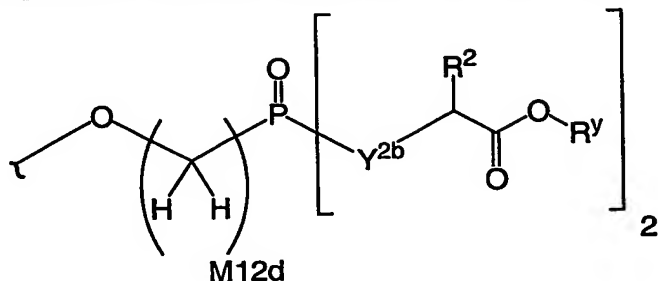65.   The compound of claim 64 wherein A^1 is of the formula:

W^{5a} is a carbocycle independently substituted with 0 or 1 R^2 groups;

A^3 is of the formula:

Y^{1a} is O or S;

Y^{2b} is O or $N(R^2)$; and

Y^{2c} is O, $N(R^y)$ or S.

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66.   The compound of claim 65 wherein A^1 is of the formula:

W^{5a} is a carbocycle independently substituted with 0 or 1 R^2 groups;

10   A^3 is of the formula:

R^1 is independently H or alkyl of 1 to 18 carbon atoms;

Y^{1a} is O or S;

15   Y^{2b} is O or $N(R^2)$;

Y^{2d} is O or $N(R^y)$; and

M12d is 1, 2, 3, 4, 5, 6, 7 or 8.

67.   The compound of claim 66 wherein A^1 is of the formula:

Y^{2b} is O or $N(R^2)$; and

M12d is 1, 2, 3, 4, 5, 6, 7 or 8.

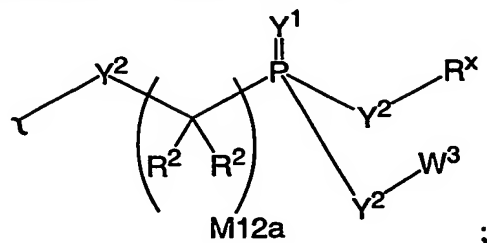68.   The compound of claim 66 wherein A^1 is of the formula:
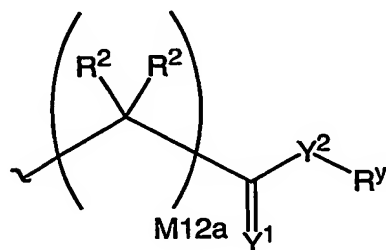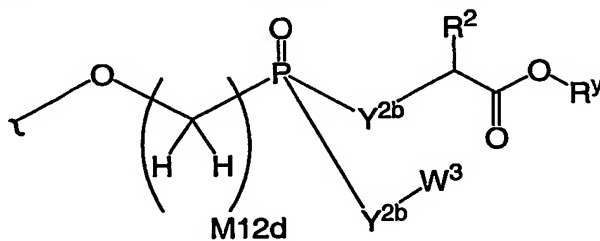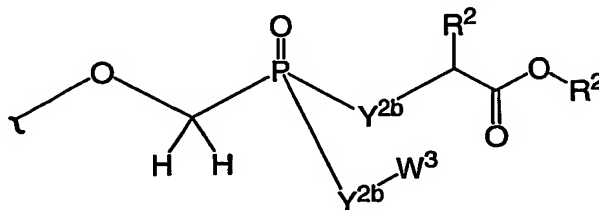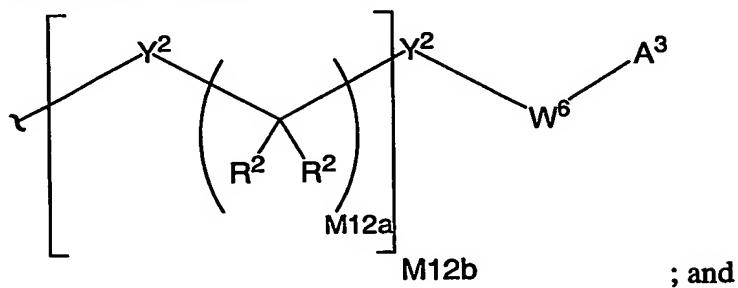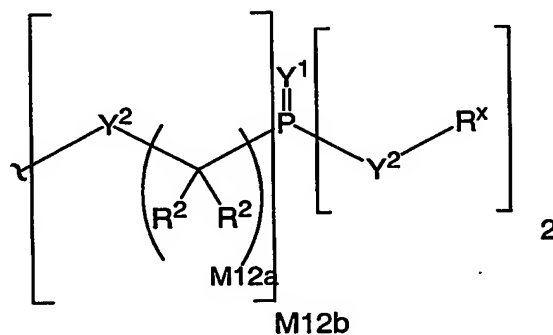

and Y^{2b} is O or $N(R^2)$; and

M12d is 1, 2, 3, 4, 5, 6, 7 or 8.

69.   The compound of claim 3 wherein A^1 is of the formula:

; and

A^3 is of the formula:

$$\left[Y^2 \cdot \left(R^2 \ R^2 \right)_{M12a} \cdot P \begin{array}{c} Y^1 \\ \| \\ \end{array} \begin{array}{c} Y^2 - R^x \\ Y^2 - W^3 \end{array} \right]_{M12b}$$

M12b .

70. The compound of claim 69 wherein A^1 is of the formula:

$$\left[Y^2 \cdot \left(R^2 \ R^2 \right)_{M12a} \cdot W^6 - A^3 \right]_{M12b} ;$$

M12b ;

A^3 is of the formula:

$$Y^2 \cdot \left(R^2 \ R^2 \right)_{M12a} \cdot P \begin{array}{c} Y^1 \\ \| \\ \end{array} \begin{array}{c} Y^2 - R^x \\ Y^2 - W^3 \end{array} ; \text{ and}$$

; and

R^x is of the formula:

$$\left(R^2 \ R^2 \right)_{M12a} \cdot \begin{array}{c} Y^2 - R^y \\ \| \\ Y^1 \end{array} .$$
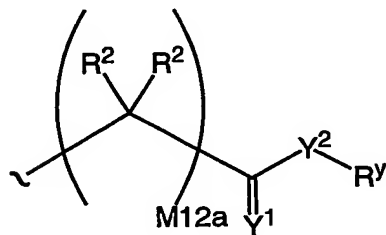
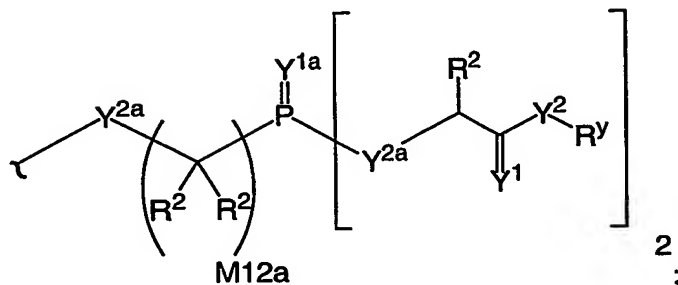71.   The compound of claim 70 wherein A^1 is of the formula:
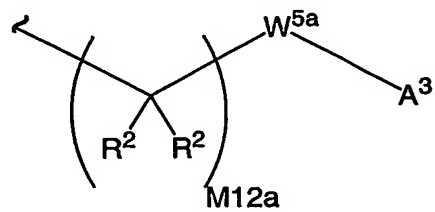

;

A^3 is of the formula:

;
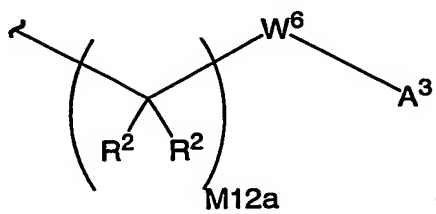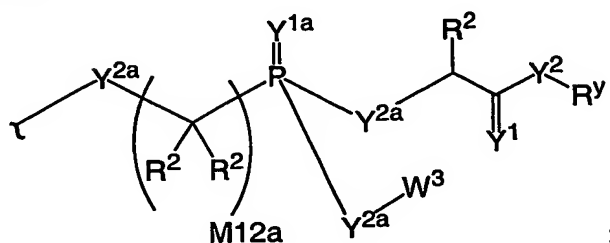
Y^{1a} is O or S; and
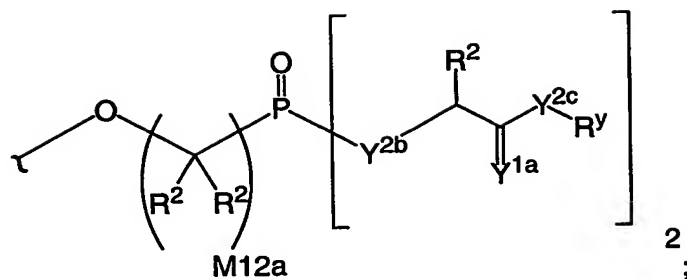
Y^{2a} is O, $N(R^2)$ or S.

72.   The compound of claim 71 wherein A^1 is of the formula:
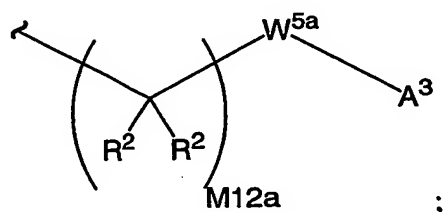
;

W^{5a} is a carbocycle independently substituted with 0 or 1 R^2 groups;
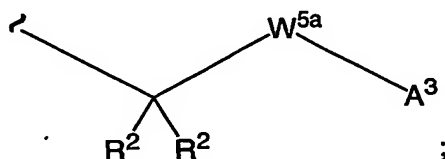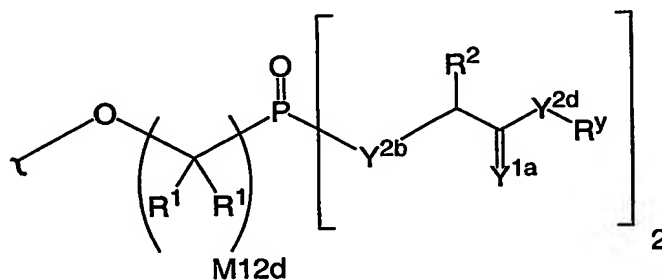
A^3 is of the formula:

;

Y^{1a} is O or S;

Y^{2b} is O or $N(R^2)$; and

Y^{2c} is O, $N(R^y)$ or S.

-1677-
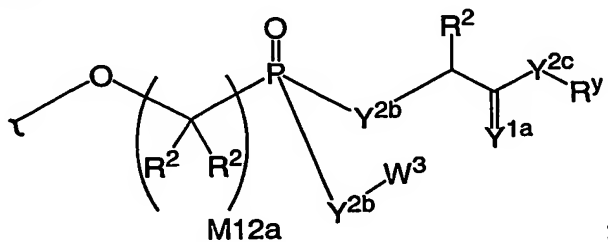
73.   The compound of claim 72 wherein A^3 is of the formula:
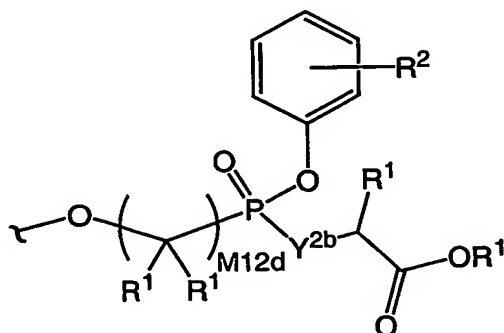
wherein R^1 is independently H or alkyl of 1 to 18 carbon atoms; and the phenyl carbocycle is substituted with 0 to 3 R^2 groups.

74.   The compound of claim 70 wherein A^1 is of the formula:
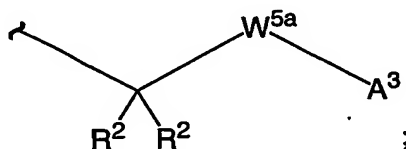
W^{5a} is a carbocycle or heterocycle where W^{5a} is independently substituted with 0 or 1 R^2 groups;
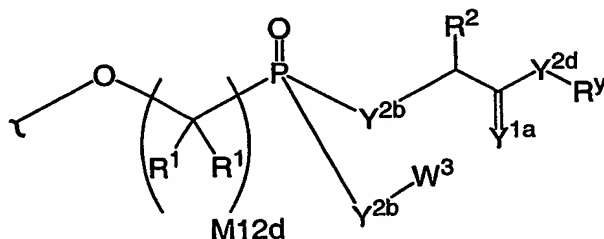
A^3 is of the formula:

Y^{1a} is O or S;

Y^{2b} is O or $N(R^2)$;

Y^{2d} is O or $N(R^y)$; and

M12d is 1, 2, 3, 4, 5, 6, 7 or 8.

75.   A compound of claim 74 wherein Y^{2b} is O and W^3 is phenyl.

76.   A compound of claim 75 wherein A^3 is of the formula:
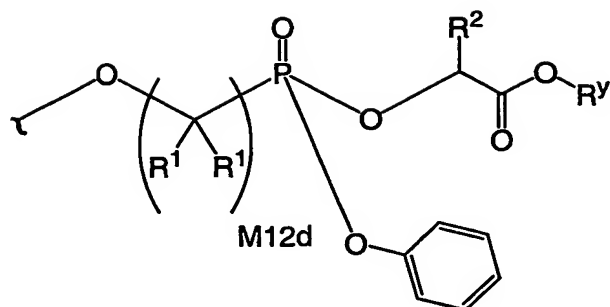
77. A compound of claim 75 wherein A^3 is of the formula:
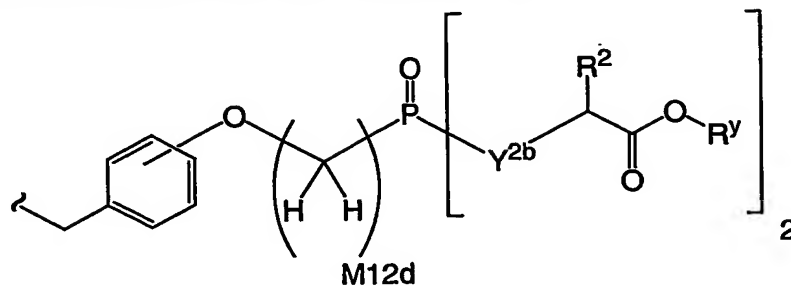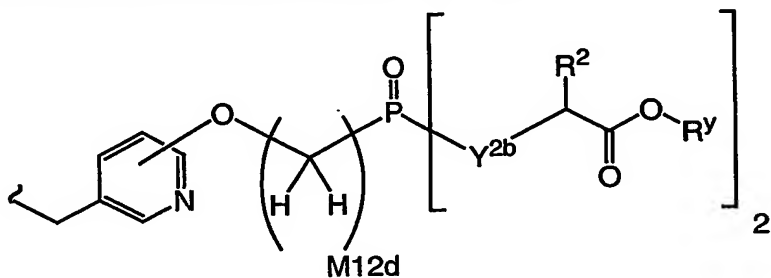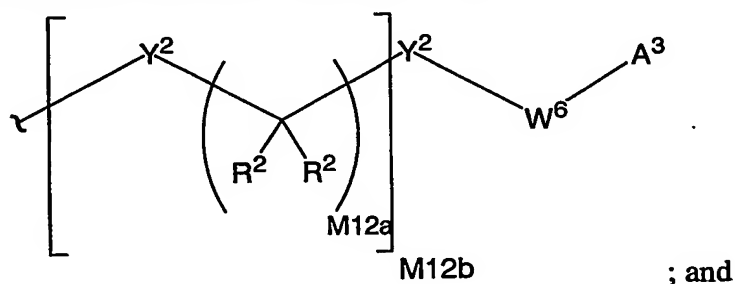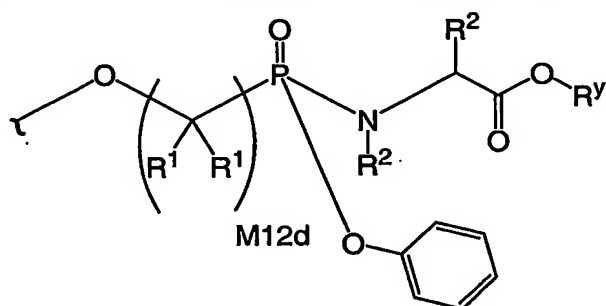

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78. A compound of claim 74 wherein A^1 is of the formula:
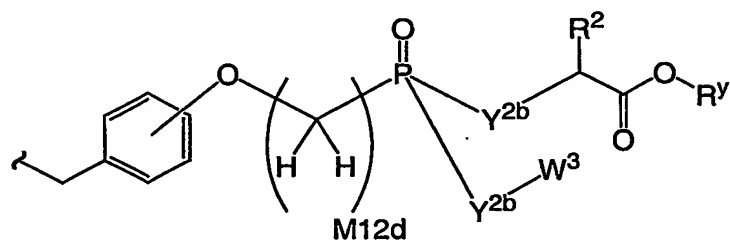
Y^{2b} is O or $N(R^2)$; and

10 M12d is 1, 2, 3, 4, 5, 6, 7 or 8.

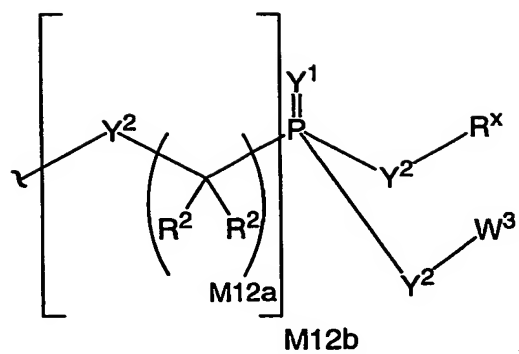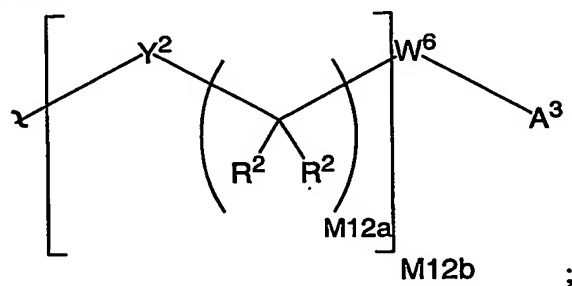79. The compound of claim 3 wherein A^2 is of the formula:

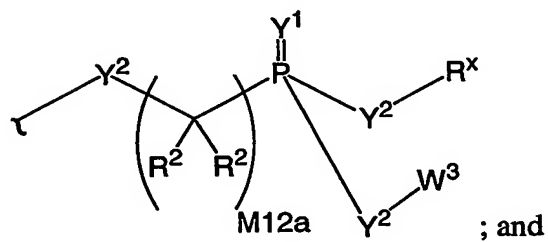$$\left[\hspace{0.3cm}\overset{Y^2}{\diagup\hspace{-0.2cm}\diagdown}\left(\underset{\underset{M12a}{R^2\ R^2}}{\hspace{0.2cm}}\right)\overset{Y^2}{\diagup\hspace{-0.2cm}\diagdown}W^5\hspace{0.3cm}\right]_{M12b}$$
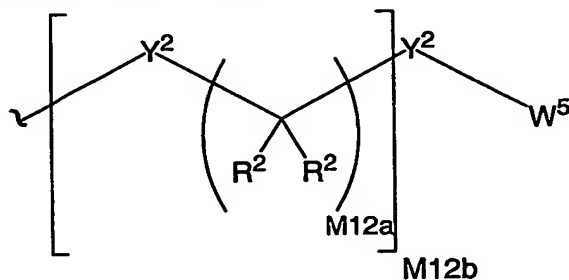
80. The compound of claim 79 wherein A^2 is of the formula:

$$\left[\hspace{0.3cm}\overset{Y^2}{\diagup\hspace{-0.2cm}\diagdown}\left(\underset{\underset{M12a}{R^2\ R^2}}{\hspace{0.2cm}}\right)\overset{W^5}{\diagup\hspace{-0.2cm}\diagdown}\hspace{0.3cm}\right]_{M12b}$$
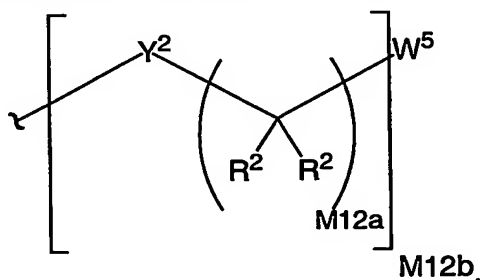
81. The compound of claim 80 wherein M12b is 1.

82. The compound of claim 80 where M12b is 0, Y^2 is a bond and W^5 is a carbocycle or heterocycle where W^5 is optionally and independently substituted with 1, 2, or 3 R^2 groups.

83. The compound of claim 80 wherein A^2 is of the formula:

$$\diagdown\hspace{-0.2cm}\diagup\left(\underset{\underset{M12a}{R^2\ R^2}}{\hspace{0.2cm}}\right)\diagdown\hspace{-0.2cm}\diagup W^{5a}\hspace{0.3cm};$$
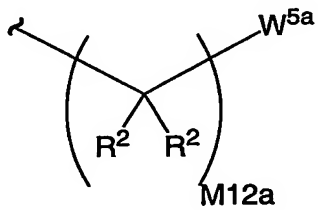
and W^{5a} is a carbocycle or heterocycle where W^{5a} is optionally and independently substituted with 1, 2, or 3 R^2 groups.

84.   The compound of claim 83 wherein M12a is 1.

85.   The compound of claim 83 wherein A^2 is selected from phenyl, substituted phenyl, benzyl, substituted benzyl, pyridyl and substituted pyridyl.

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86.   The compound of claim 3 wherein A^2 is of the formula:
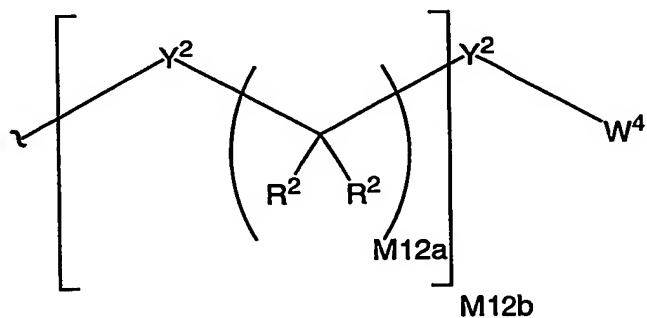
87.   The compound of claim 86 wherein A^2 is of the formula:
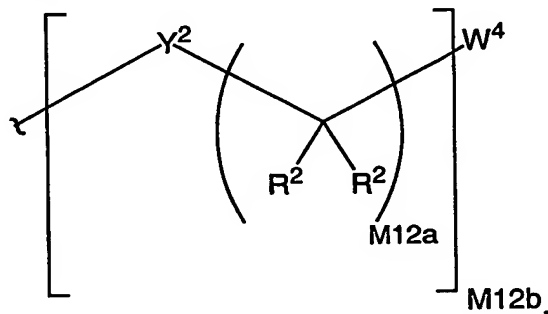
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88.   The compound of claim 87 wherein M12b is 1.

89.   A Formula II compound of claim 5 having the formula:
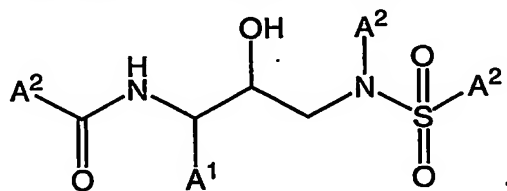
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90.   A compound of claim 89 having the formula:
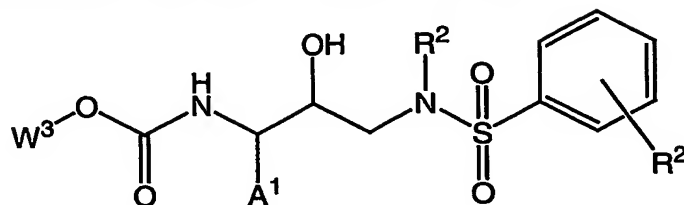
91.   A compound of claim 90 having the formula:
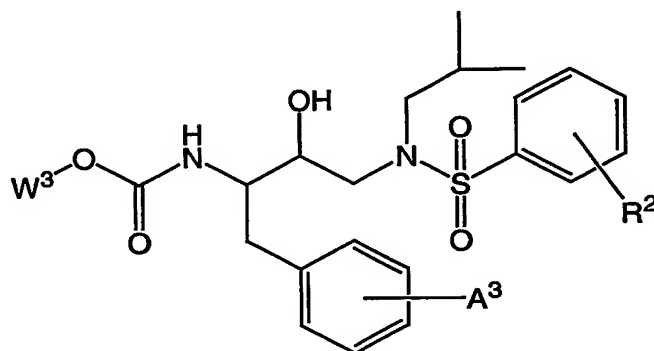
92.   A compound of the formula MBF.

93.   A compound of claim 92 having the formula:
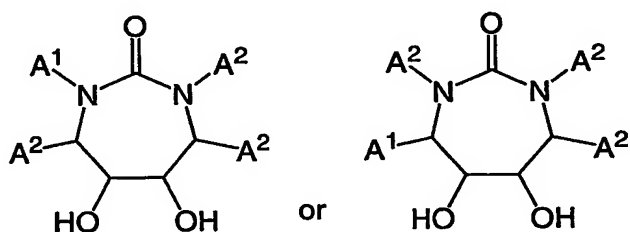
94.   The compound of claim 93 wherein A^2 is selected from benzyl, substituted benzyl, heterocycle and substituted heterocycle.

95.   A compound of claim 3 wherein A^1 is of the formula:
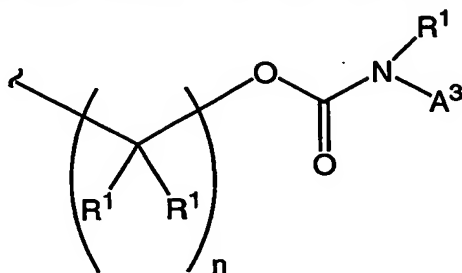
R¹ is independently H or alkyl of 1 to 18 carbon atoms; and n is an integer from 1 to 18; A^3 is of the formula:
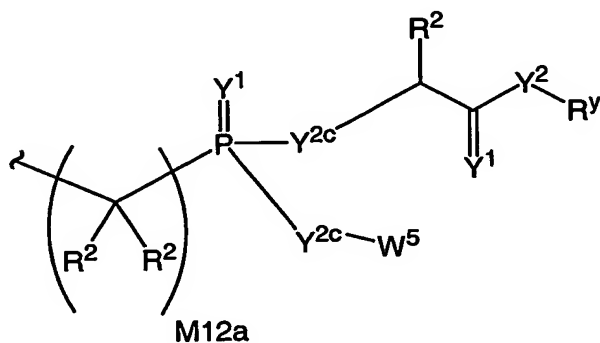
and Y^{2c} is O, N(R^y) or S.

96.   The compound of claim 95 wherein R^1 is H and n is 1.

97.   A compound of claim 91 having the formula:
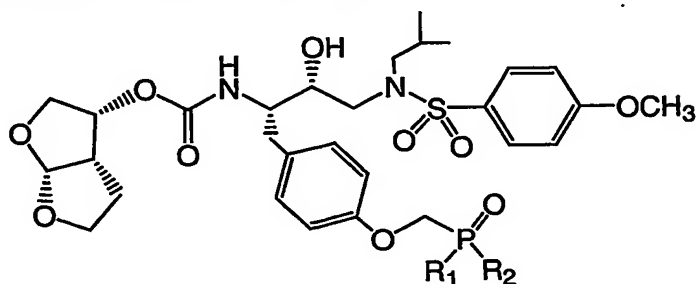
wherein R_1 and R_2 are independently selected from hydroxy, methoxy, ethoxy, trifluoroethoxy, isopropoxy, phenoxy, benzyloxy, and O-pivaloyloxymethyl.

98.   A compound of claim 91 having the formula:

wherein R_1 and R_2 are independently selected from hydroxy, methoxy, ethoxy, trifluoroethoxy, isopropoxy, phenoxy, benzyloxy, and O-pivaloyloxymethyl.

99.   A compound of claim 91 having the formula:

wherein R_1 and R_2 are independently selected from hydroxy, methoxy, ethoxy, trifluoroethoxy, isopropoxy, phenoxy, benzyloxy, and O-pivaloyloxymethyl.

100.   A compound of claim 91 having the formula:

wherein R_1 and R_2 are independently selected from hydroxy, methoxy, ethoxy, trifluoroethoxy, isopropoxy, phenoxy, benzyloxy, and O-pivaloyloxymethyl.

101.   A compound of claim 91 having the formula:

wherein R_1 and R_2 are independently selected from $-NR$ where R is C_1-C_6 alkyl or an amino acid ester.

102.   The compound of claim 101 wherein R_1 and R_2 are independently selected from $-NMe$, $-NEt$, Gly-Et, Ala-Et, Aba-Et, Val-Et, Leu-Et, Phe-Bu, and Phe-Et.

103.   A compound of claim 91 having the formula:

or
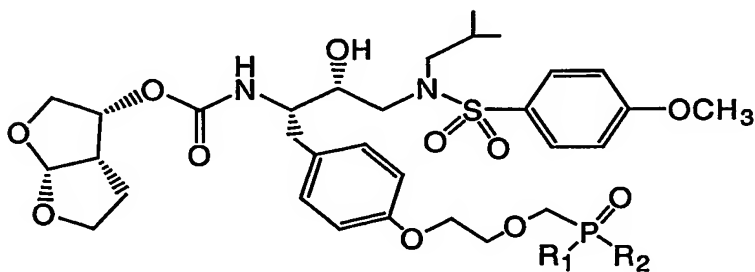
wherein R_1 and R_2 are independently selected from hydroxy, methoxy, ethoxy, trifluoroethoxy, isopropoxy, phenoxy, benzyloxy, O-pivaloyloxymethyl, and a lactate ester.

104.   The compound of claim 103 wherein R_1 is hydroxy, methoxy, ethoxy, trifluoroethoxy, isopropoxy, phenoxy, substituted phenoxy or benzyloxy; and R_2 is Glc-Et, Lac-Me, Lac-Et, Lac-iPr, Lac-Bu, Lac-EtMor, Lac-Me, Lac-Et, Lac-Bn, Lac-Bn, Lac-OH, Lac-OH, Hba-Et, Hba-tBu, Hba-OH, MeBut-Et, or DiMePro-Me.

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105.   A compound of claim 104 where the lactate ester is the (R) configuration.

106.   A compound of claim 104 where the lactate ester is the (S) configuration.

10   107.   A compound of claim 91 having the formula:
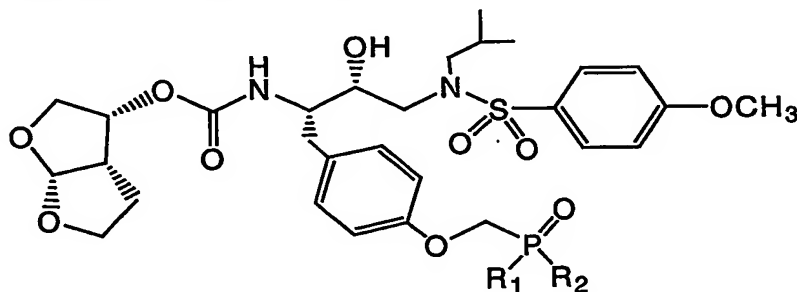
wherein R_1 is phenoxy, benzyloxy, ethoxy, trifluoroethoxy, or hydroxyl; and R_2 is an amino acid ester.

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108.   The compound of claim 107 wherein the amino acid ester is selected from Gly-Bu, Ala-Me, Ala-Et, Ala-iPr, (D)Ala-iPr, Ala-Bu, Aba-Et, Aba-Bu, and Ala-OH.

109.   A compound of claim 91 having the formula:
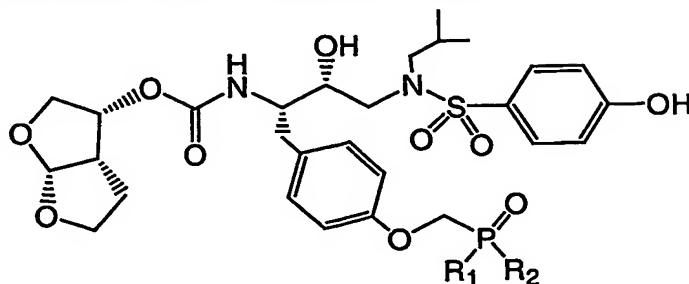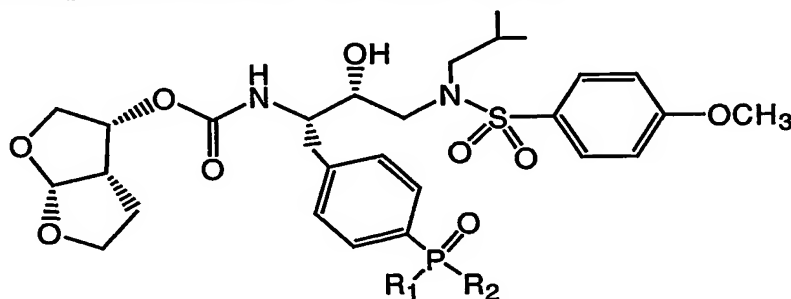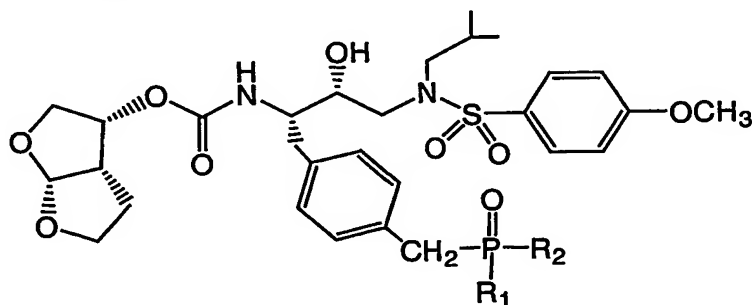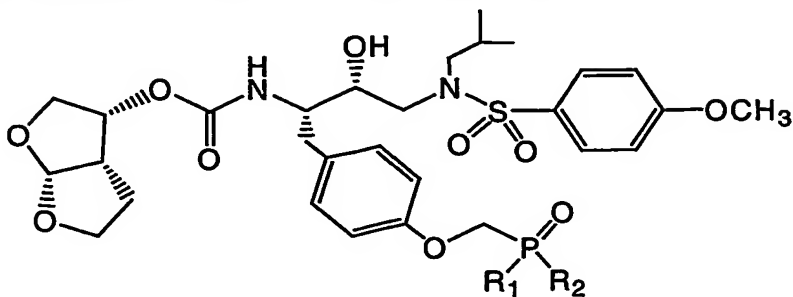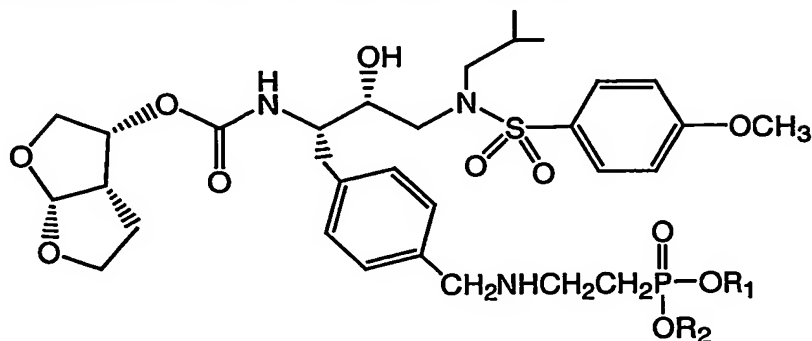

wherein R_1 and R_2 are independently selected from hydroxy, methoxy, ethoxy,
trifluoroethoxy, isopropoxy, phenoxy, benzyloxy, O-pivaloyloxymethyl, an amino acid ester
and a lactate ester.

110.   The compound of claim 109 wherein R_1 is hydroxy, methoxy, ethoxy,
trifluoroethoxy, isopropoxy, phenoxy, substituted phenoxy or benzyloxy; and R_2 is a lactate
ester selected from Glc-Et, Lac-Me, Lac-Et, Lac-iPr, Lac-Bu, Lac-EtMor, Lac-Me, Lac-Et,
Lac-Bn, Lac-Bn, Lac-OH, Lac-OH, Hba-Et, Hba-tBu, Hba-OH, MeBut-Et, and DiMePro-
Me.

111.   The compound of claim 109 wherein R_1 is hydroxy, methoxy, ethoxy,
trifluoroethoxy, isopropoxy, phenoxy, substituted phenoxy or benzyloxy; and R_2 is an amino
acid ester is selected from Gly-Bu, Ala-Me, Ala-Et, Ala-iPr, (D)Ala-iPr, Ala-Bu, Aba-Et,
Aba-Bu, and Ala-OH.

112.   A compound of claim 5 having the formula:

wherein A^1 is selected from the formulas:
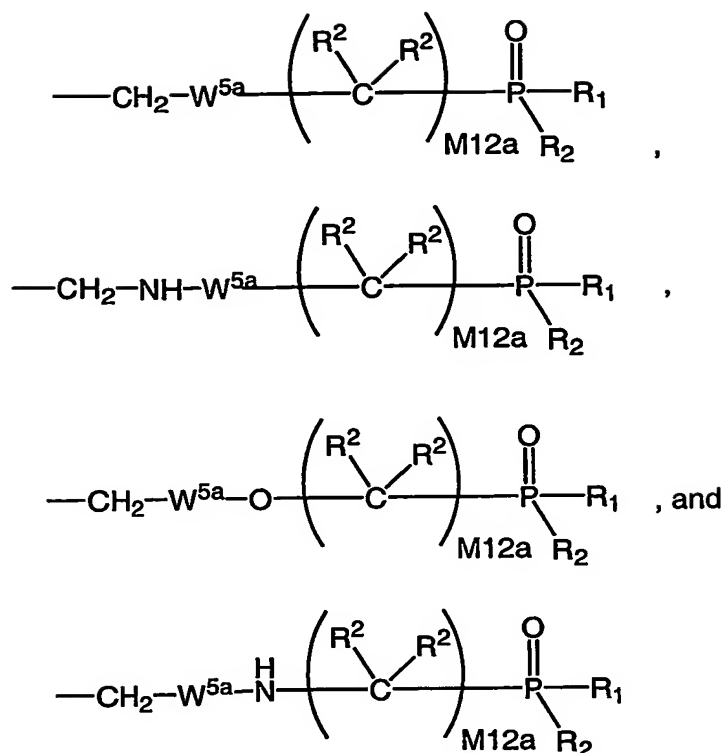
$$—CH_2—W^{5a}\left(\begin{array}{c}R^2 \quad R^2\\ C\\ M12a\end{array}\right)\overset{O}{\underset{R_2}{P}}—R_1 \quad,$$

$$—CH_2—NH—W^{5a}\left(\begin{array}{c}R^2 \quad R^2\\ C\\ M12a\end{array}\right)\overset{O}{\underset{R_2}{P}}—R_1 \quad,$$

$$—CH_2—W^{5a}—O\left(\begin{array}{c}R^2 \quad R^2\\ C\\ M12a\end{array}\right)\overset{O}{\underset{R_2}{P}}—R_1 \quad, \text{and}$$

$$—CH_2—W^{5a}—\overset{H}{N}\left(\begin{array}{c}R^2 \quad R^2\\ C\\ M12a\end{array}\right)\overset{O}{\underset{R_2}{P}}—R_1$$

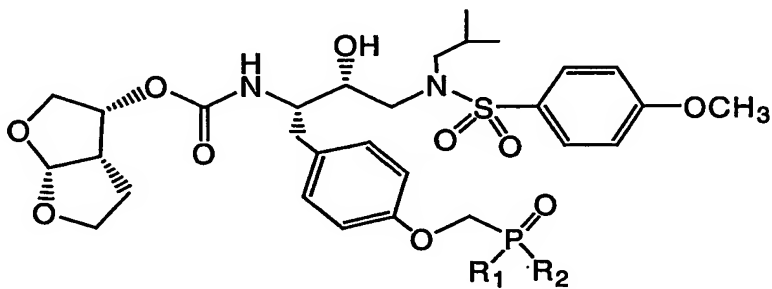R_1 and R_2 are independently selected from hydroxy, methoxy, ethoxy, trifluoroethoxy, isopropoxy, phenoxy, benzyloxy, O-pivaloyloxymethyl, an amino acid ester and a lactate ester; and

5   W^{5a} is selected from the formulas:
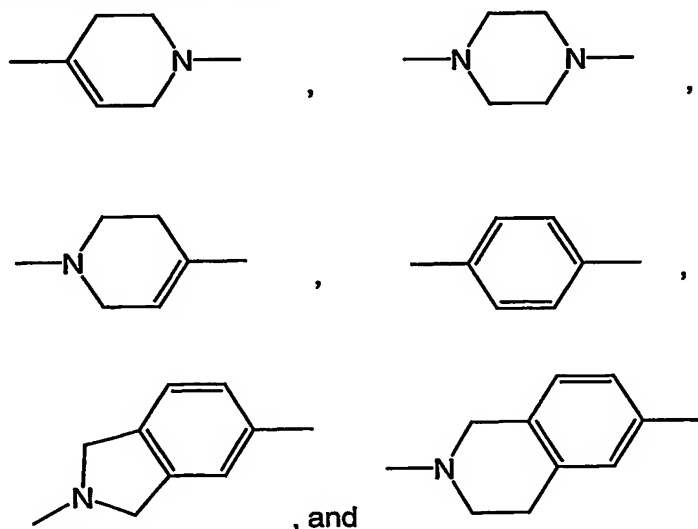
113.   A compound of claim 112 wherein A^1 is selected from the formulas:

$$-CH_2-N \begin{array}{c} \\ N \end{array} \begin{array}{c} O \\ \| \\ P-OEt \\ | \\ OEt \end{array} \quad ,$$

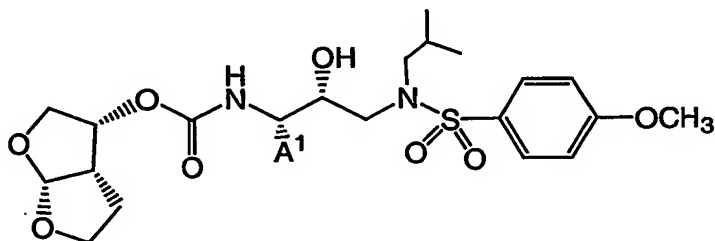$$-CH_2-N \begin{array}{c} \\ \end{array} O \begin{array}{c} O \\ \| \\ P-OEt \\ | \\ OEt \end{array} \quad , \text{ and}$$

$$-CH_2 \begin{array}{c} \\ \end{array} N-CH_2 \begin{array}{c} O \\ \| \\ P-OH \\ | \\ OH \end{array} \quad .$$
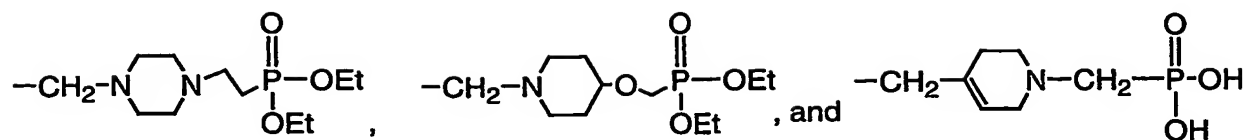
114.   A compound of claim 94 having the structure:
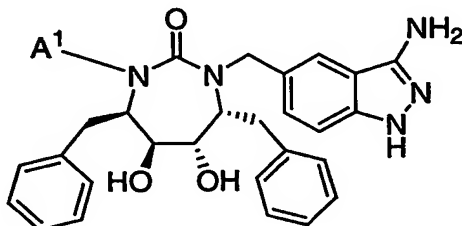
5

115.   A compound of claim 114 having the structure:
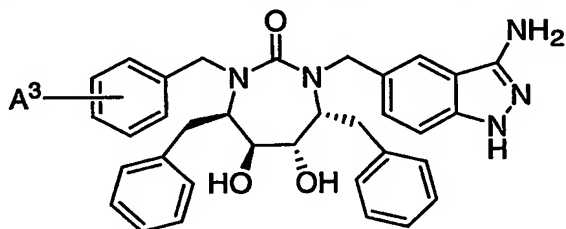
wherein the ortho, meta, or para carbon of the phenyl ring is substituted with A^3.

116. A compound of claim 115 wherein A³ is of the formula:

M12a
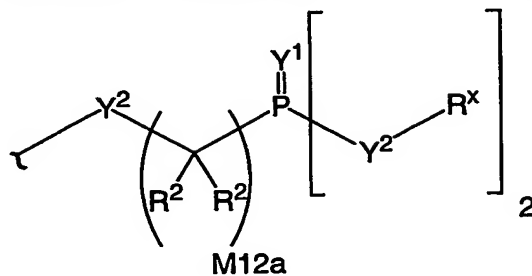
117. A compound of claim 115 wherein A³ is of the formula:

5

M12a

M12b
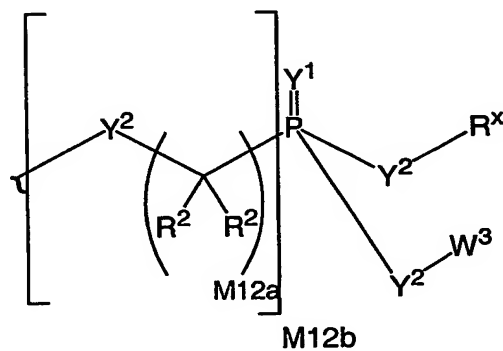
118. A compound of claim 114 wherein A¹ is of the formula:

M12a

10
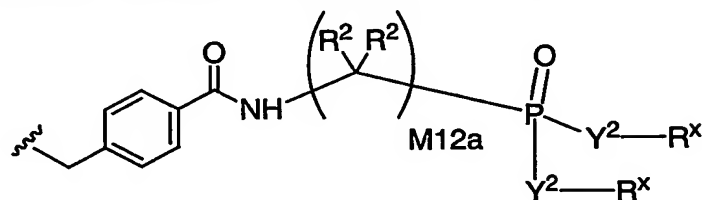
119. A compound of claim 118 wherein Y^2 is O, R^2 is H, and R^x is C_1–C_6 alkyl.

120. A compound of claim 118 wherein A^1 is of the formula:
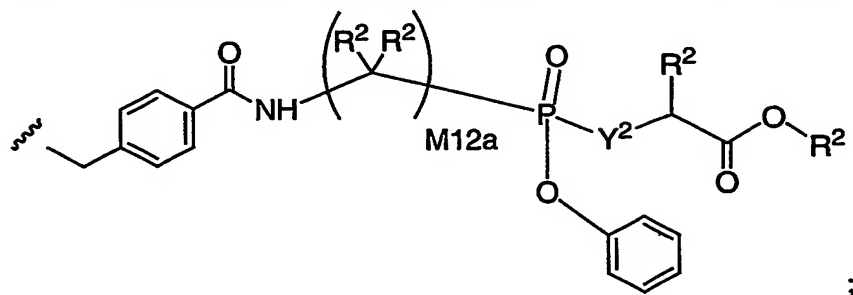
and Y^2 is O, NH, or NR^4.

121. A Formula VIIIa compound of claim 3 having the structure:
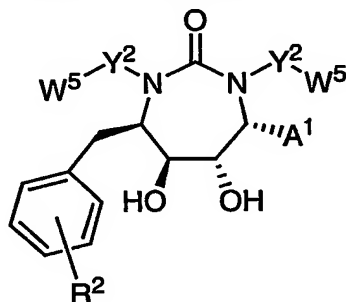
122. A Formula VIIIa compound of claim 3 having the structure:

123.   A compound selected from the Formulas:

I

II   X = C, SO

III

IV

V

VI

VII

VIIIa

VIIIb

VIIIc   and   VIIId;

-1692-
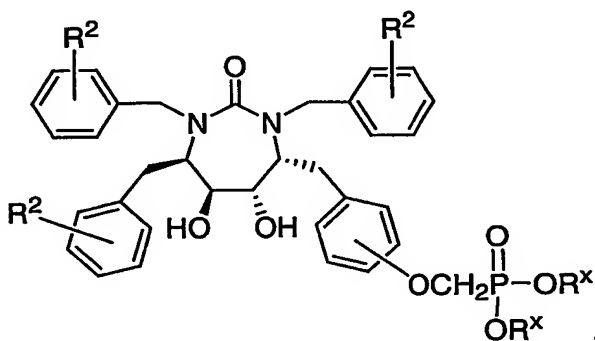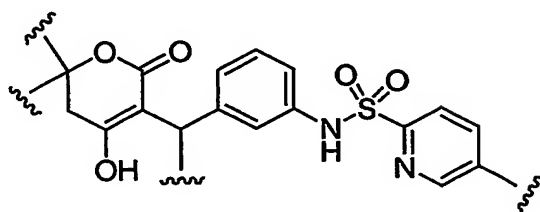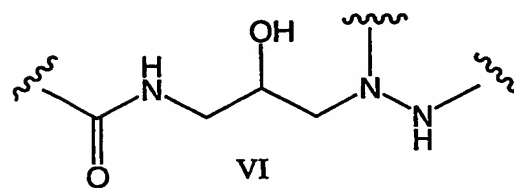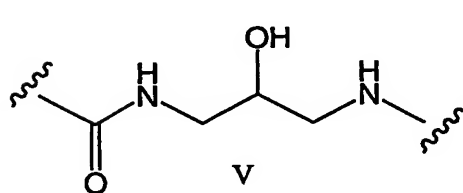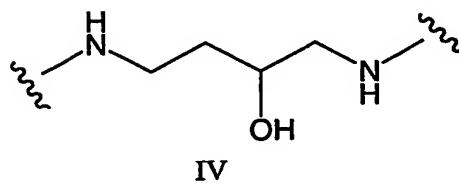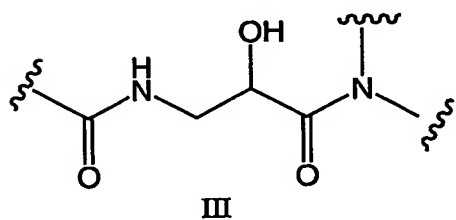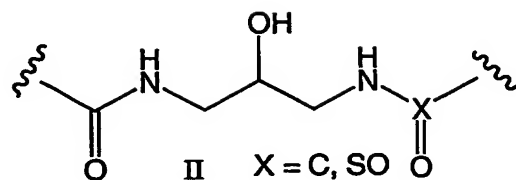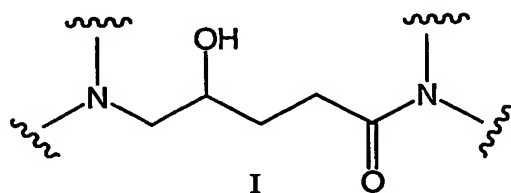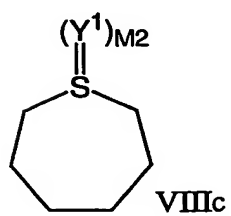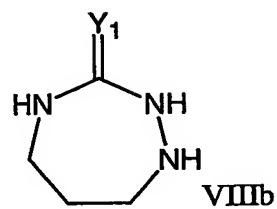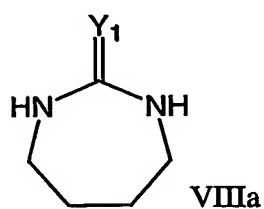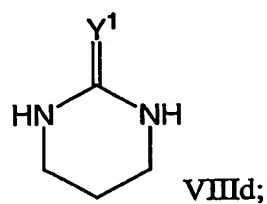
wherein Formulas I, II, III, IV, V, VI, VII and VIIIa-d are substituted with one or more covalently attached A_1 groups, and optionally substituted with one or more covalently attached A_2 groups;

A_1 is $-(X_2-(C(R_2)(R_2))_{m1}-X_3)_{m1}-W_3$, wherein W_3 is substituted with 1 to 3 A_3 groups;

A_2 is $-(X_2-(C(R_2)(R_2))_{m1}-X_3)_{m1}-W_3$;

A_3 is $-(X_2-(C(R_2)(R_2))_{m1}-X_3)_{m1}-P(Y_1)(Y_1R_{6a})(Y_1R_{6a})$; `

X_2 and X_3 are independently a bond, -O-, $-N(R_2)-$, $-N(OR_2)-$, $-N(N(R_2)(R_2))-$, -S-, -SO-, or $-SO_2-$;

each Y_1 is independently O, $N(R_2)$, $N(OR_2)$, or $N(N(R_2)(R_2))$, wherein each Y_1 is bound by two single bonds or one double bond;

R_1 is independently H or alkyl of 1 to 12 carbon atoms;

R_2 is independently H, R_3 or R_4 wherein each R_4 is independently substituted with 0 to 3 R_3 groups;

R_3 is independently F, Cl, Br, I, -CN, N_3, $-NO_2$, $-OR_{6a}$, $-OR_1$, $-N(R_1)_2$, $-N(R_1)(R_{6b})$, $-N(R_{6b})_2$, $-SR_1$, $-SR_{6a}$, $-S(O)R_1$, $-S(O)_2R_1$, $-S(O)OR_1$, $-S(O)OR_{6a}$, $-S(O)_2OR_1$, $-S(O)_2OR_{6a}$, $-C(O)OR_1$, $-C(O)R_{6c}$, $-C(O)OR_{6a}$, $-OC(O)R_1$, $-N(R_1)(C(O)R_1)$, $-N(R_{6b})(C(O)R_1)$, $-N(R_1)(C(O)OR_1)$, $-N(R_{6b})(C(O)OR_1)$, $-C(O)N(R_1)_2$, $-C(O)N(R_{6b})(R_1)$, $-C(O)N(R_{6b})_2$, $-C(NR_1)(N(R_1)_2)$, $-C(N(R_{6b}))(N(R_1)_2)$, $-C(N(R_1))(N(R_1)(R_{6b}))$, $-C(N(R_{6b}))(N(R_1)(R_{6b}))$, $-C(N(R_1))(N(R_{6b})_2)$, $-C(N(R_{6b}))(N(R_{6b})_2)$, $-N(R_1)C(N(R_1))(N(R_1)_2)$, $-N(R_1)C(N(R_1))(N(R_1)(R_{6b}))$, $-N(R_1)C(N(R_{6b}))(N(R_1)_2)$, $-N(R_{6b})C(N(R_1))(N(R_1)_2)$, $-N(R_{6b})C(N(R_{6b}))(N(R_1)_2)$, $-N(R_{6b})C(N(R_1))(N(R_1)(R_{6b}))$, $-N(R_1)C(N(R_{6b}))(N(R_1)(R_{6b}))$, $-N(R_1)C(N(R_1))(N(R_{6b})_2)$, $-N(R_{6b})C(N(R_{6b}))(N(R_1)(R_{6b}))$, $-N(R_{6b})C(N(R_1))(N(R_{6b})_2)$, $-N(R_1)C(N(R_{6b}))(N(R_{6b})_2)$, $-N(R_{6b})C(N(R_{6b}))(N(R_{6b})_2)$, =O, =S, $=N(R_1)$, $=N(R_{6b})$ or W_5;

R_4 is independently alkyl of 1 to 12 carbon atoms, alkenyl of 2 to 12 carbon atoms, or alkynyl of 2 to 12 carbon atoms;

R_5 is independently R_4 wherein each R_4 is substituted with 0 to 3 R_3 groups; or R_5 is independently alkylene of 1 to 12 carbon atoms, alkenylene of 2 to 12 carbon atoms, or

alkynylene of 2-12 carbon atoms any one of which alkylene, alkenylene or alkynylene is substituted with 0-3 R3 groups;

R_{6a} is independently H or an ether- or ester-forming group;

R_{6b} is independently H, a protecting group for amino or the residue of a carboxyl-

5   containing compound;

R_{6c} is independently H or the residue of an amino-containing compound;

W_3 is W_4 or W_5;

W_4 is R_5, -C(Y_1)R_5, -C(Y_1)W_5, -SO_2R_5, or -SO_2W_5;

W_5 is carbocycle or heterocycle wherein W_5 is independently substituted with 0 to 3

10   R_2 groups;

$m1$ is independently an integer from 0 to 12, wherein the sum of all $m1$'s within each individual claim of A_1, A_2 or A_3 is 12 or less;

$m2$ is independently an integer from 0 to 2; and

$\mathcal{r}^{\mathcal{S}}$ indicates a site of covalent attachment of A_1 or A_2.

15

124.   The compound of claim 123 wherein:

A_1 is -(C(R_2)(R_2))_{m1}-W_3, wherein W_3 is substituted with 1 A_3 group;

A_2 is -(C(R_2)(R_2))_{m1}-W_3; and

A_3 is -(C(R_2)(R_2))_{m1}-P(Y_1)(Y_1R_{6a})(Y_1R_{6a}).

20

125.   The compound of claim 123 wherein W_3 is W_5, and W_5 is selected from: ·
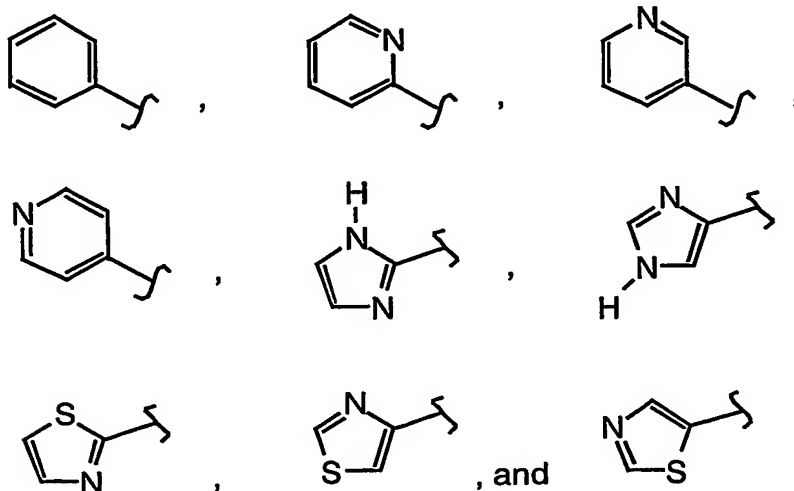
126.   The compound of claim 125 wherein W_5 is a pyridine heterocycle bonded to —$C(R_2)_2$— at the 2, 3, 4, 5 or 6 position.

5   127.   The compound of claim 125 wherein A_3 has a formula selected from:
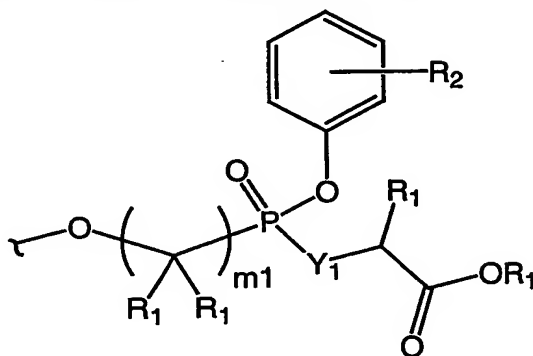
wherein ml is 1, 2, 3, 4, 5, 6, 7 or 8, and the phenyl carbocycle is substituted with 0 to 3 R_2 groups.

10   128.   The compound of claim 125 wherein A_3 has a formula selected from:

129. The compound of claim 128 wherein A₃ has a formula selected from:

130. A method of inhibiting the activity of HIV protease comprising the step of
5   contacting a sample suspected of containing HIV with a composition of claim 1.

131. The method of claim 130 wherein the HIV protease is *in vivo*.
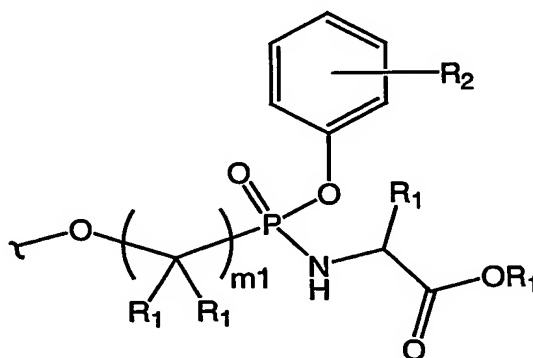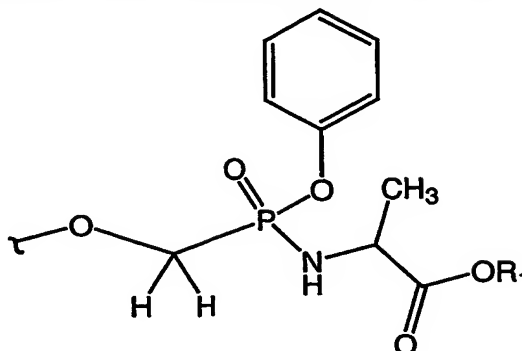
132. A method for the treatment or prevention of the symptoms or effects of HIV
10   infection in an animal which comprises administering to said animal a formulation
comprising a therapeutically effective amount of a compound according to claim 1.

133. The method of claim 132 wherein the compound is formulated with a
pharmaceutically acceptable carrier.
15

134. The use of a compound of claim 1 to prepare a medicament for treatment of
AIDS.

135. The use of a compound of claim 3 to prepare a medicament for treatment of
20   AIDS.

136. The method of claim 133 wherein the formulation further comprises a second
active ingredient selected from a nucleotide reverse transcriptase inhibitor, a non-nucleoside
reverse transcriptase inhibitor, an HIV protease inhibitor, and an HIV integrase inhibitor.

25

137.   A process for preparing a compound of claim 1 wherein a compound comprising A^3 or a precursor to A^3 is reacted with an HIV protease inhibitor compound wherein the HIV protease inhibitor compound does not have a phosphonate group, whereby a compound of claim 1 is formed.

5

138.   In an HIV protease inhibitor, the improvement comprising a substituent having a phosphonate or phosphonate prodrug.

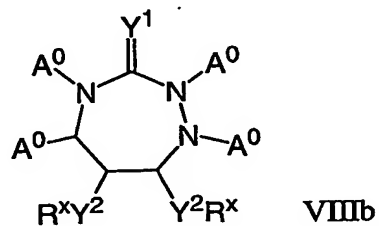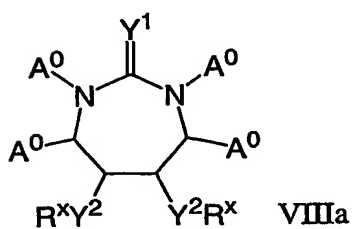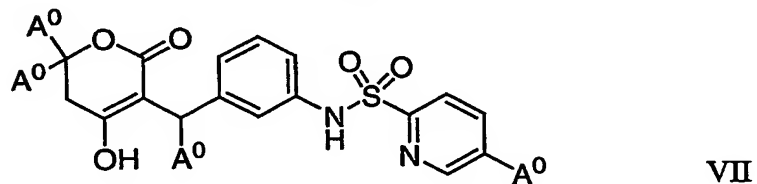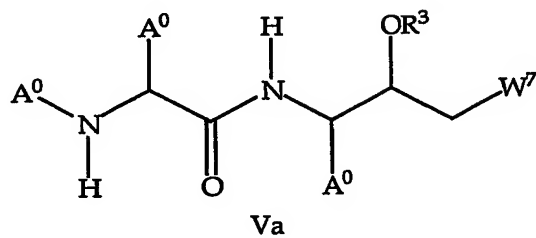139.   The improved HIV protease inhibitor compound of claim 138 selected from:

10   a Saquinavir-like phosphonate protease inhibitor compound,

a Lopinavir-like phosphonate protease inhibitor compound,

a Ritonavir-like phosphonate protease inhibitor compound,

a Indinavir-like phosphonate protease inhibitor compound,

a Atazanavir-like phosphonate protease inhibitor compound,

15   a Nelfinavir-like phosphonate protease inhibitor compound,

a Tipranavir-like phosphonate protease inhibitor compound,

a Amprenavir-like phosphonate protease inhibitor compound,

a KNI-like phosphonate protease inhibitor compound, and

a Cyclic Carbonyl-like phosphonate protease inhibitor compound;

20   and pharmaceutically acceptable salts, hydrates, and formulations thereof.

140. The improved HIV protease inhibitor compound of claim 138 of the Formulas:

I

II   X = C, SO

III

IV

V

VI

Va

VII

VIIIa

VIIIb

5

VIIIc and VIIId;

wherein:

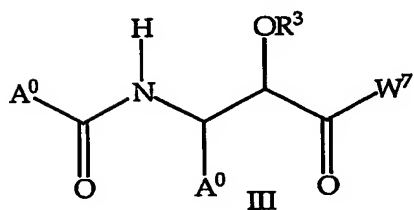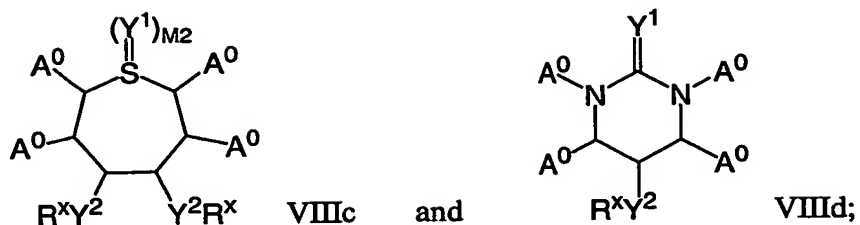A⁰ is A¹, A² or W³ with the proviso that the compound includes at least one A¹;

A¹ is:

A² is:

A³ is:

Y^1 is independently O, S, N(R^x), N(O)(R^x), N(OR^x), N(O)(OR^x), or N(N(R^x)(R^x));

Y^2 is independently a bond, O, N(R^x), N(O)(R^x), N(OR^x), N(O)(OR^x), N(N(R^x)(R^x)),

-S(O)$_{M2}$-, or -S(O)$_{M2}$-S(O)$_{M2}$-;

R^x is independently H, R^1, W^3, a protecting group, or the formula:

R^y is independently H, W^3, R^2 or a protecting group;

R^1 is independently H or an alkyl of 1 to 18 carbon atoms;

R^2 is independently H, R^1, R^3 or R^4 wherein each R^4 is independently substituted with 0 to 3 R^3 groups, or taken together at a carbon atom, two R^2 groups form a ring of 3 to 8 carbons and the ring may be substituted with 0 to 3 R^3 groups;

R^3 is R^{3a}, R^{3b}, R^{3c} or R^{3d}, provided that when R^3 is bound to a heteroatom, then R^3 is R^{3c} or R^{3d};

R^{3a} is F, Cl, Br, I, -CN, N_3 or -NO_2;

R^{3b} is Y^1;

R^{3c} is -R^x, -$N(R^x)(R^x)$, -SR^x, -$S(O)R^x$, -$S(O)_2R^x$, -$S(O)(OR^x)$, -$S(O)_2(OR^x)$, -$OC(Y^1)R^x$, -$OC(Y^1)OR^x$, -$OC(Y^1)(N(R^x)(R^x))$, -$SC(Y^1)R^x$, -$SC(Y^1)OR^x$, -$SC(Y^1)(N(R^x)(R^x))$, -$N(R^x)C(Y^1)R^x$, -$N(R^x)C(Y^1)OR^x$, or -$N(R^x)C(Y^1)(N(R^x)(R^x))$;

R^{3d} is -$C(Y^1)R^x$, -$C(Y^1)OR^x$ or -$C(Y^1)(N(R^x)(R^x))$;

R^4 is an alkyl of 1 to 18 carbon atoms, alkenyl of 2 to 18 carbon atoms, or alkynyl of 2 to 18 carbon atoms;

R^5 is R^4 wherein each R^4 is substituted with 0 to 3 R^3 groups;

W^3 is W^4 or W^5;

W^4 is R^5, -$C(Y^1)R^5$, -$C(Y^1)W^5$, -SO_2R^5, or -SO_2W^5;

W^5 is carbocycle or heterocycle wherein W^5 is independently substituted with 0 to 3 R^2 groups;

W^6 is W^3 independently substituted with 1, 2, or 3 A^3 groups;

W^7 is a heterocycle bonded through a nitrogen atom of said heterocycle and independently substituted with 0, 1 or 2 A^0 groups;

M2 is 0, 1 or 2;

M12a is 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11 or 12;

M12b is 0, 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11 or 12;

M1a, M1c, and M1d are independently 0 or 1; and

-1700-

M12c is 0, 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11 or 12.

141.   The improved HIV protease inhibitor compound of claim 140 of the Formulas:

5
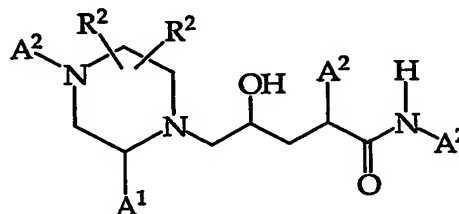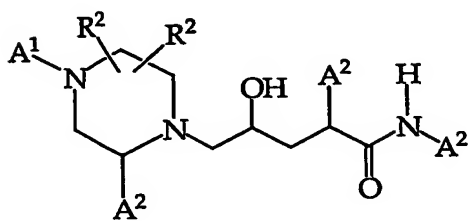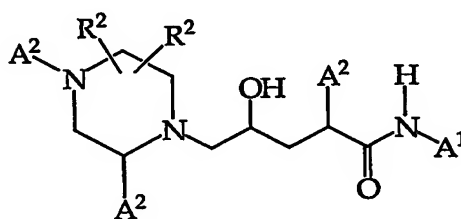
142.   The improved HIV protease inhibitor compound of claim 140 of the Formulas:

5   143.   The improved HIV protease inhibitor compound of claim 140 of the Formulas:

, and

.

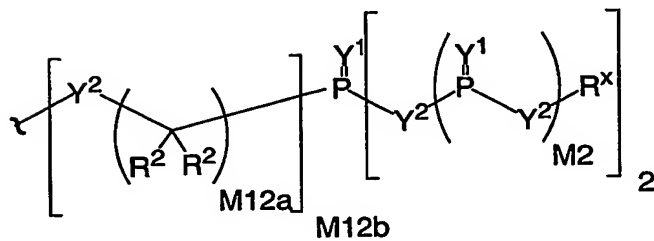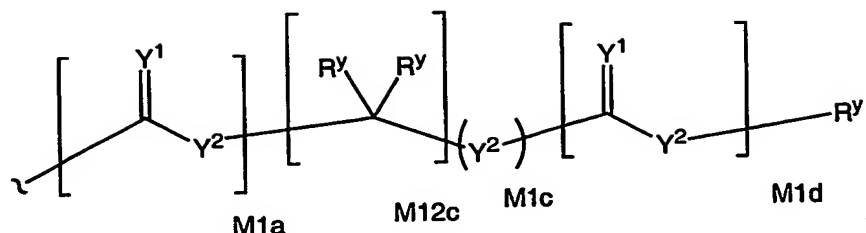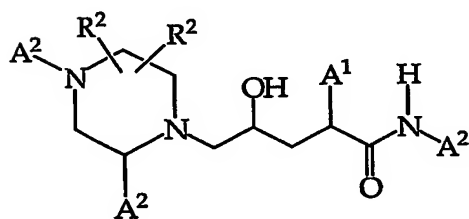144.   The improved HIV protease inhibitor compound of claim 140 of the Formulas:

,

,

and

.

5   145.   The improved HIV protease inhibitor compound of claim 140 of the Formulas:

,

,

,

and

146.   The improved HIV protease inhibitor compound of claim 140 of the Formulas:

and

and

5

147.   The improved HIV protease inhibitor compound of claim 140 of the Formulas:

and

148. The improved HIV protease inhibitor compound of claim 140 of the Formulas:

and
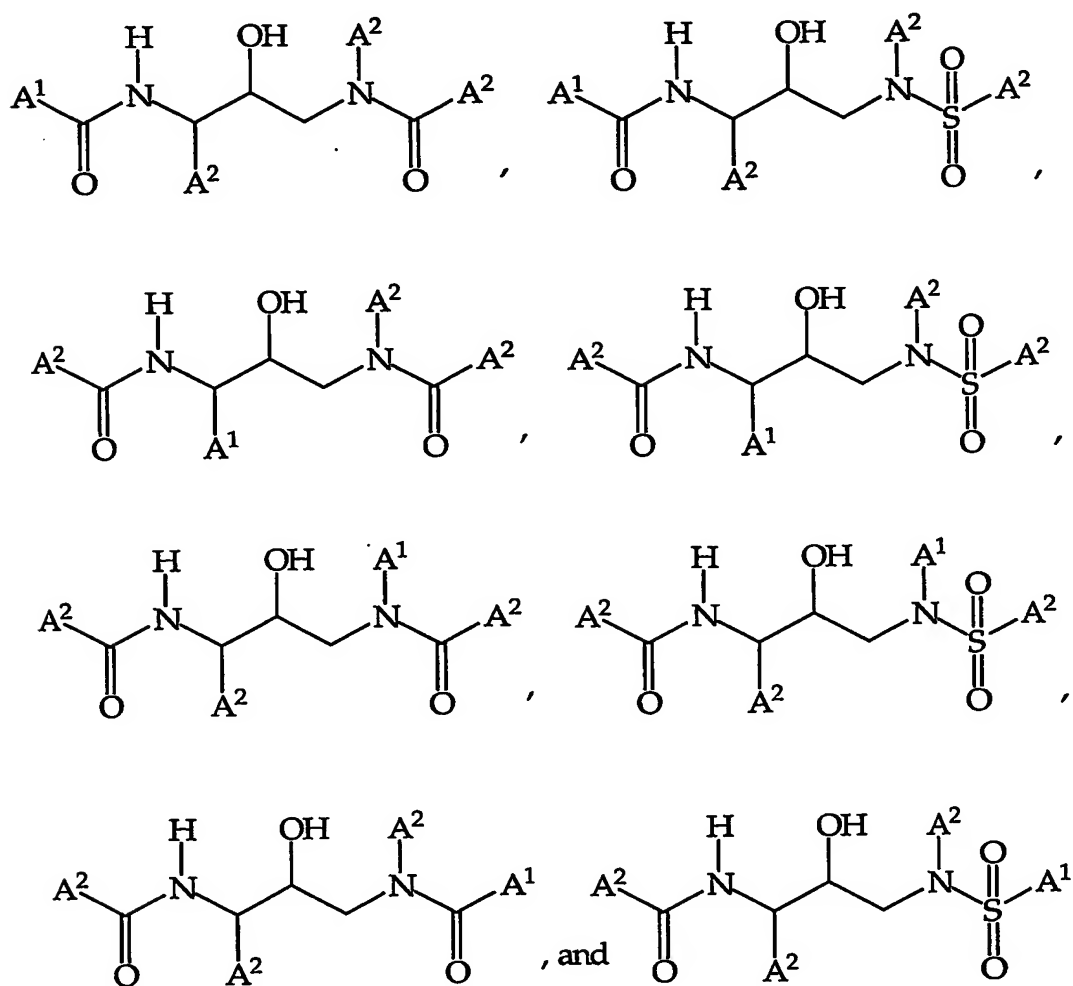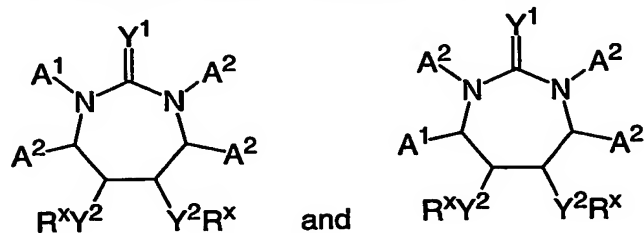
149. The improved HIV protease inhibitor compound of claim 140 of the Formulas:

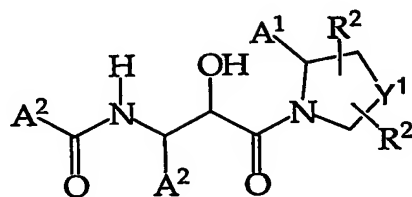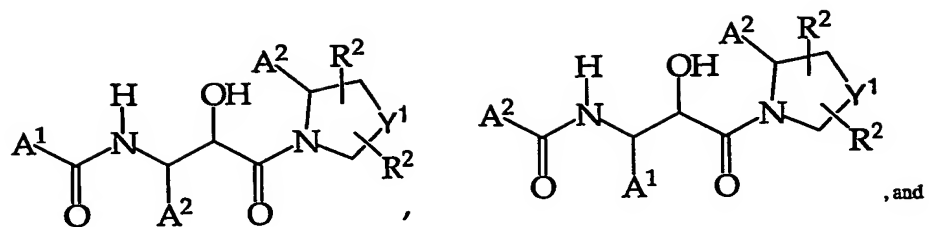and
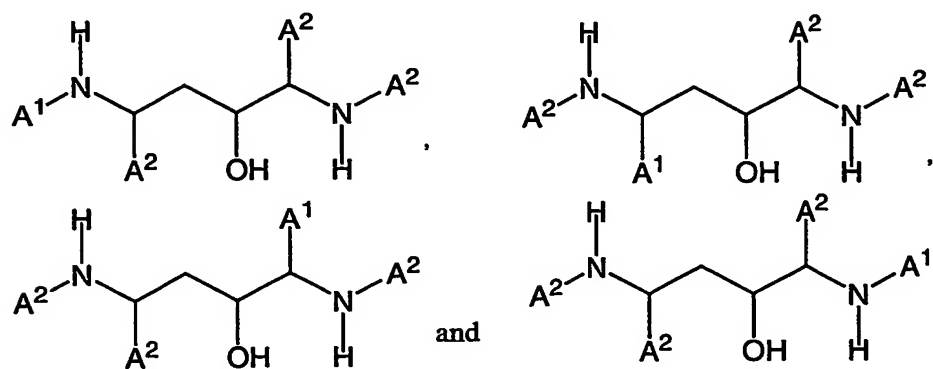
150. The improved HIV protease inhibitor compound of claim 140 of the Formulas:

and
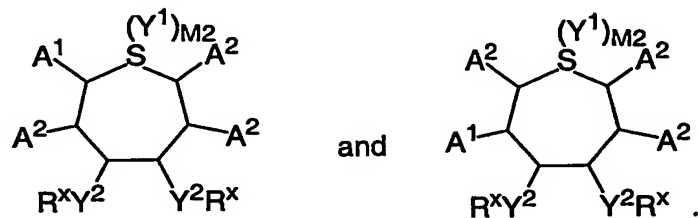
5

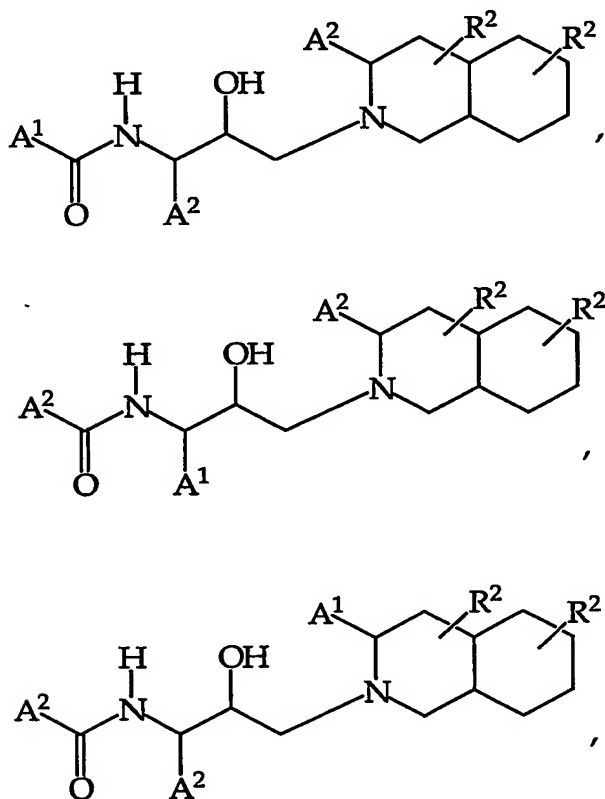151. The improved HIV protease inhibitor compound of claim 140 of the Formulas:
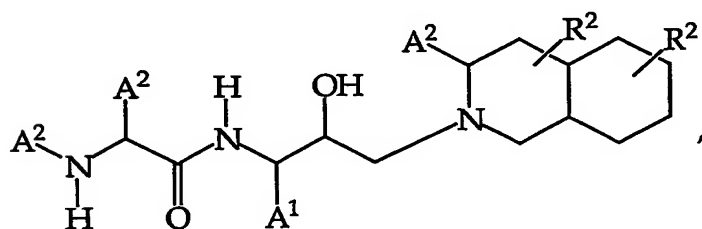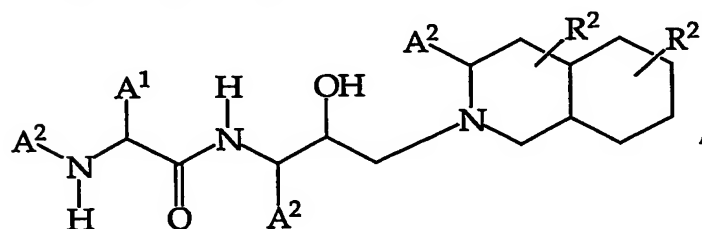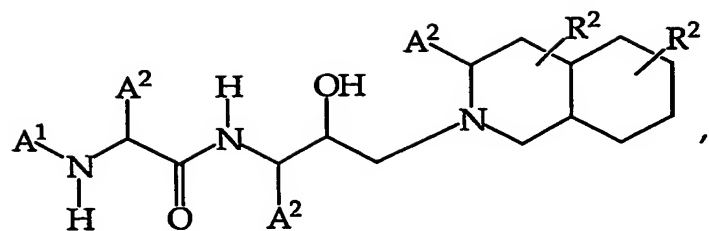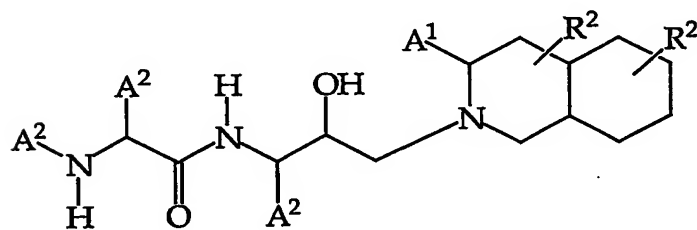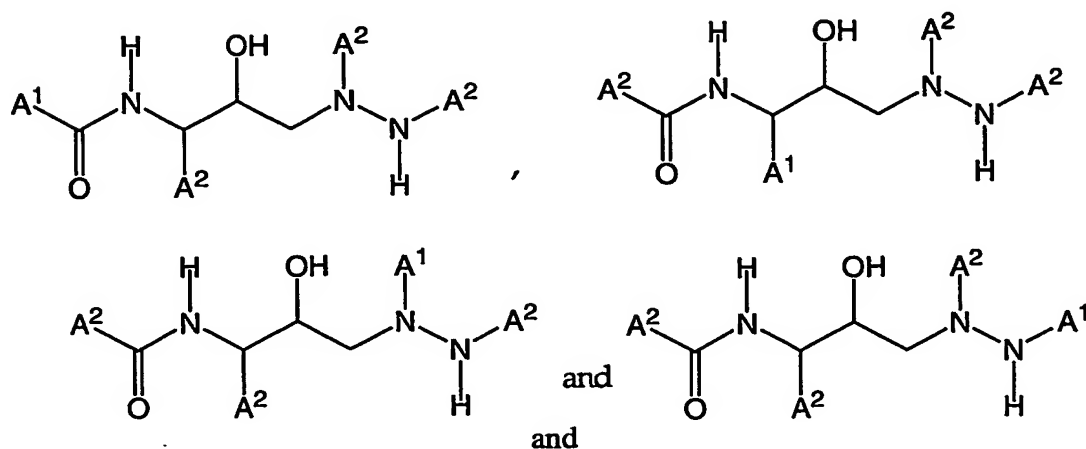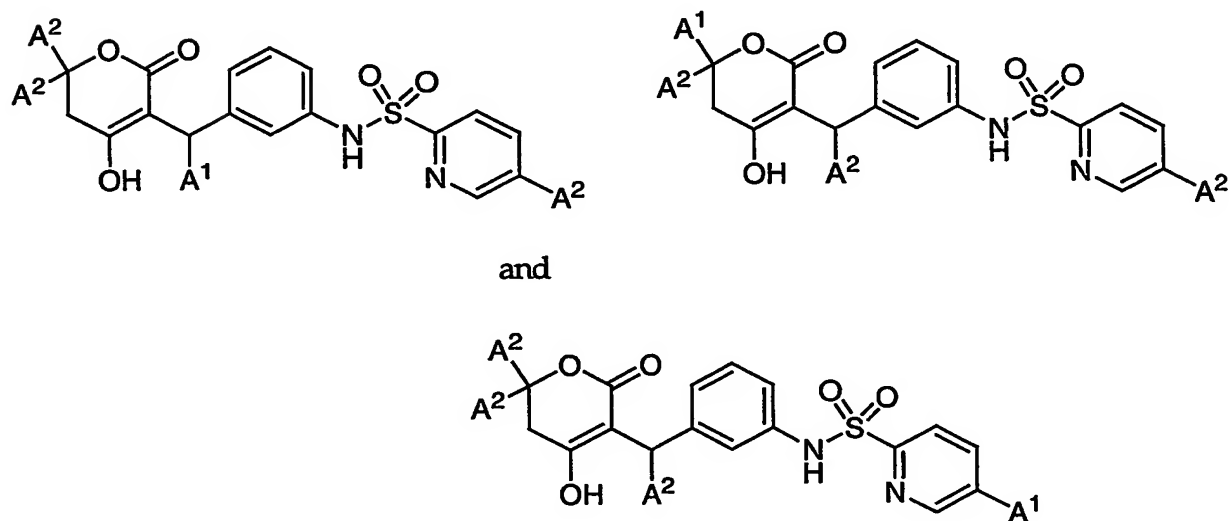

and

.
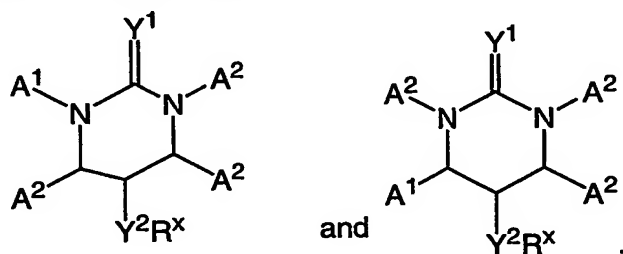
152.   In an HIV protease inhibitor not containing a phosphonate or phosphonate prodrug, the improvement comprising a substituent having a phosphonate or phosphonate prodrug.

5   153.   The improved HIV protease inhibitor compound of claim 152 selected from:
        a Saquinavir-like phosphonate protease inhibitor compound,
        à Lopinavir-like phosphonate protease inhibitor compound,
        a Ritonavir-like phosphonate protease inhibitor compound,
        a Indinavir-like phosphonate protease inhibitor compound,
10   a Atazanavir-like phosphonate protease inhibitor compound,
        a Nelfinavir-like phosphonate protease inhibitor compound,
        a Tipranavir-like phosphonate protease inhibitor compound,
        a Amprenavir-like phosphonate protease inhibitor compound,
        a KNI-like phosphonate protease inhibitor compound, and
15   a Cyclic Carbonyl-like phosphonate protease inhibitor compound;
and pharmaceutically acceptable salts, hydrates, and formulations thereof.

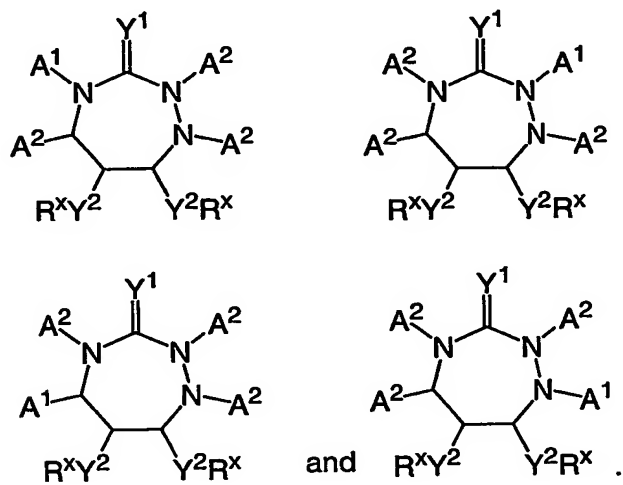154. The improved HIV protease inhibitor compound of claim 152 of the Formulas:

I

II X = C, SO

III

IV

V

VI

Va

VII

VIIIa

VIIIb

5

wherein:

A^0 is A^1, A^2 or W^3 with the proviso that the compound includes at least one A^1;

A^1 is:

A^2 is:

A^3 is:

Y^1 is independently O, S, $N(R^x)$, $N(O)(R^x)$, $N(OR^x)$, $N(O)(OR^x)$, or $N(N(R^x)(R^x))$;

Y^2 is independently a bond, O, $N(R^x)$, $N(O)(R^x)$, $N(OR^x)$, $N(O)(OR^x)$, $N(N(R^x)(R^x))$, $-S(O)_{M2}-$, or $-S(O)_{M2}-S(O)_{M2}-$;

R^x is independently H, R^1, W^3, a protecting group, or the formula:

R^y is independently H, W^3, R^2 or a protecting group;

R^1 is independently H or an alkyl of 1 to 18 carbon atoms;

R^2 is independently H, R^1, R^3 or R^4 wherein each R^4 is independently substituted with

0 to 3 R^3 groups, or taken together at a carbon atom, two R^2 groups form a ring of 3 to 8

carbons and the ring may be substituted with 0 to 3 R^3 groups;

R^3 is R^{3a}, R^{3b}, R^{3c} or R^{3d}, provided that when R^3 is bound to a heteroatom, then R^3 is

R^{3c} or R^{3d};

R^{3a} is F, Cl, Br, I, -CN, N_3 or -NO_2;

R^{3b} is Y^1;

R^{3c} is -R^x, -$N(R^x)(R^x)$, -SR^x, -$S(O)R^x$, -$S(O)_2R^x$, -$S(O)(OR^x)$, -$S(O)_2(OR^x)$,

-$OC(Y^1)R^x$, -$OC(Y^1)OR^x$, -$OC(Y^1)(N(R^x)(R^x))$, -$SC(Y^1)R^x$, -$SC(Y^1)OR^x$,

-$SC(Y^1)(N(R^x)(R^x))$, -$N(R^x)C(Y^1)R^x$, -$N(R^x)C(Y^1)OR^x$, or -$N(R^x)C(Y^1)(N(R^x)(R^x))$;

R^{3d} is -$C(Y^1)R^x$, -$C(Y^1)OR^x$ or -$C(Y^1)(N(R^x)(R^x))$;

R^4 is an alkyl of 1 to 18 carbon atoms, alkenyl of 2 to 18 carbon atoms, or alkynyl of

2 to 18 carbon atoms;

R^5 is R^4 wherein each R^4 is substituted with 0 to 3 R^3 groups;

W^3 is W^4 or W^5;

W^4 is R^5, -$C(Y^1)R^5$, -$C(Y^1)W^5$, -SO_2R^5, or -SO_2W^5;

W^5 is carbocycle or heterocycle wherein W^5 is independently substituted with 0 to 3

R^2 groups;

W^6 is W^3 independently substituted with 1, 2, or 3 A^3 groups;

W^7 is a heterocycle bonded through a nitrogen atom of said heterocycle and

independently substituted with 0, 1 or 2 A^0 groups;

M2 is 0, 1 or 2;

M12a is 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11 or 12;

M12b is 0, 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11 or 12;

M1a, M1c, and M1d are independently 0 or 1; and

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M12c is 0, 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11 or 12.

155.   The improved HIV protease inhibitor compound of claim 154 of the Formulas:

5

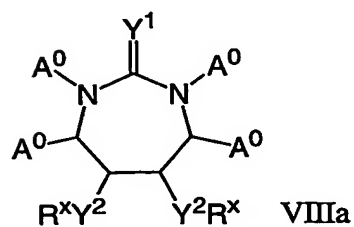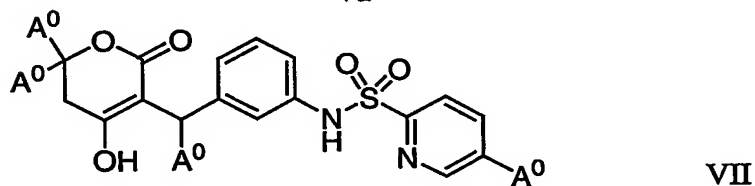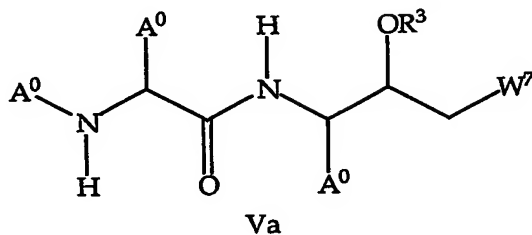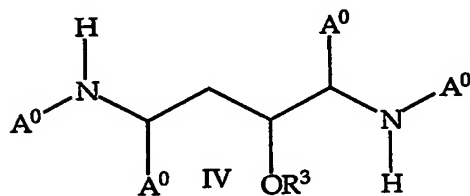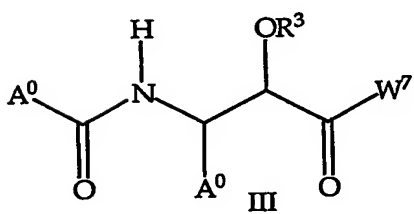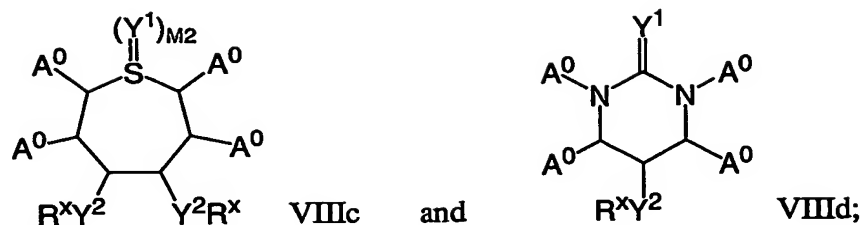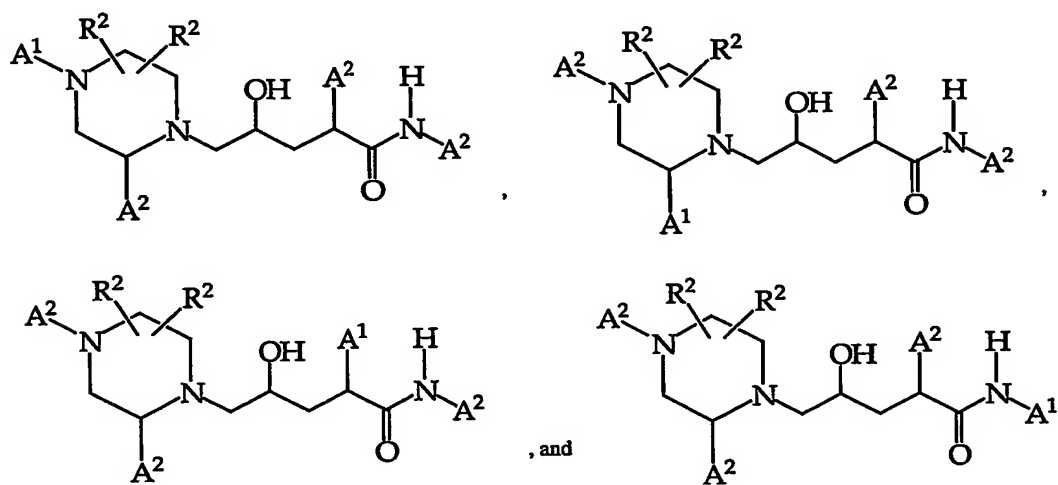156. The improved HIV protease inhibitor compound of claim 154 of the Formulas:
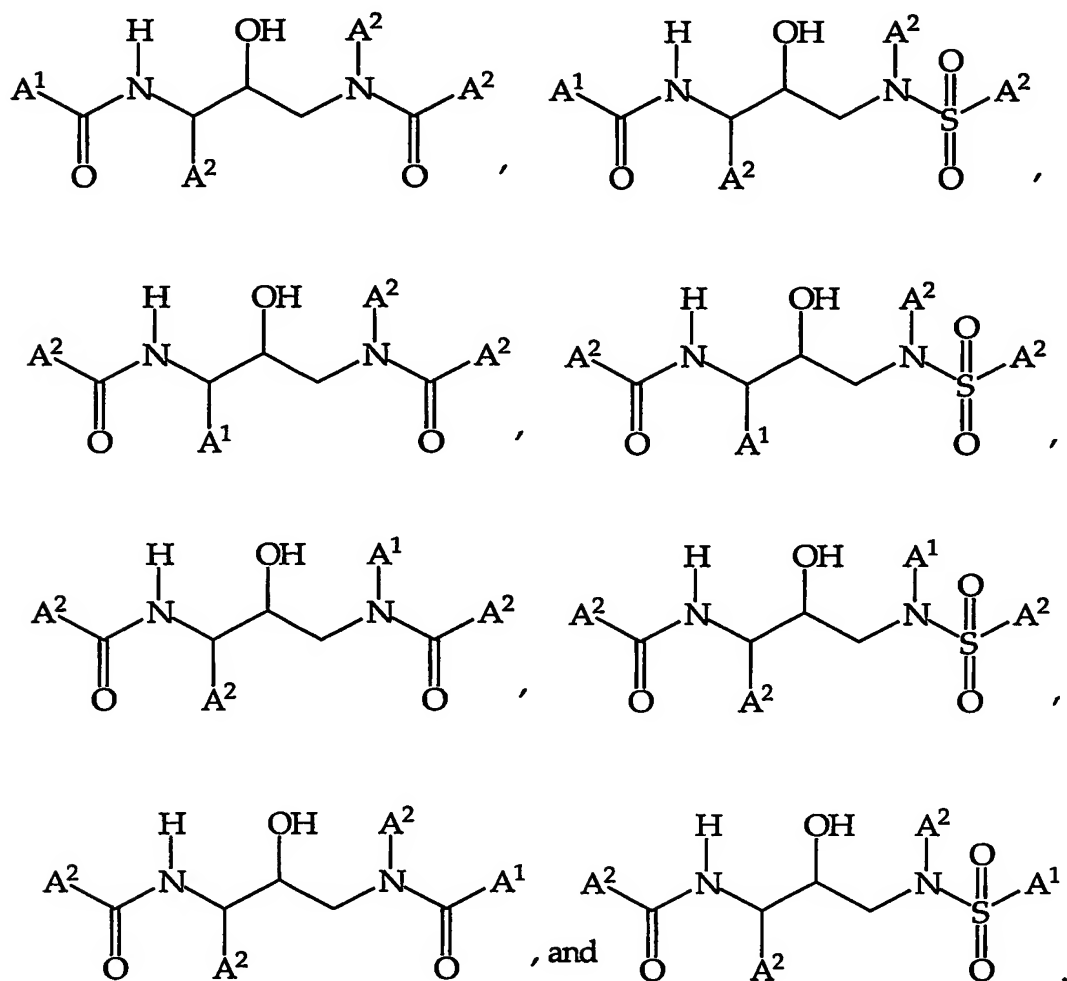
5   157. The improved HIV protease inhibitor compound of claim 154 of the Formulas:

, and
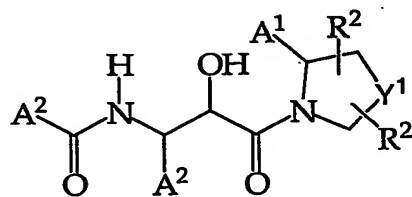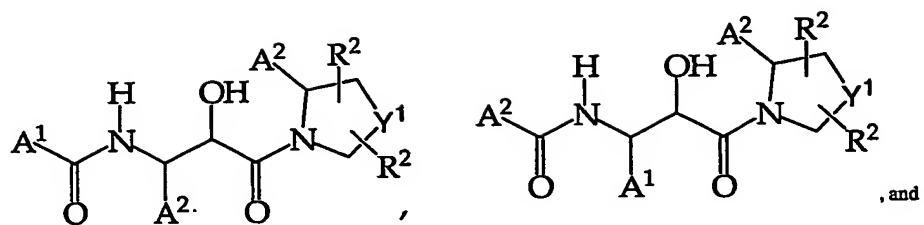
158.   The improved HIV protease inhibitor compound of claim 154 of the Formulas:
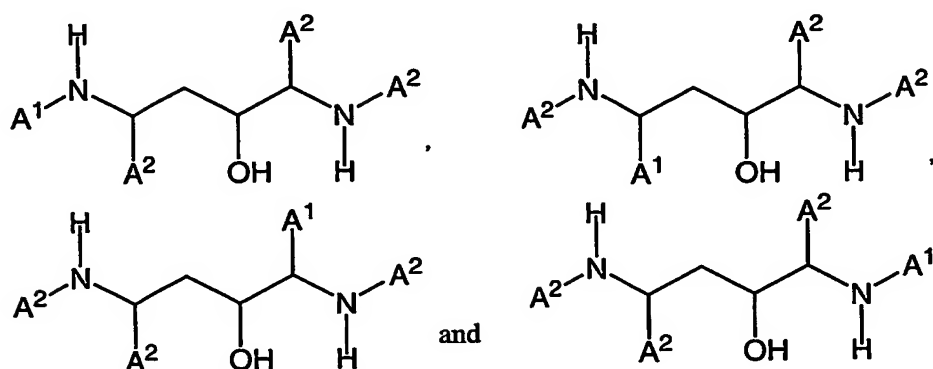
159.   The improved HIV protease inhibitor compound of claim 154 of the Formulas:
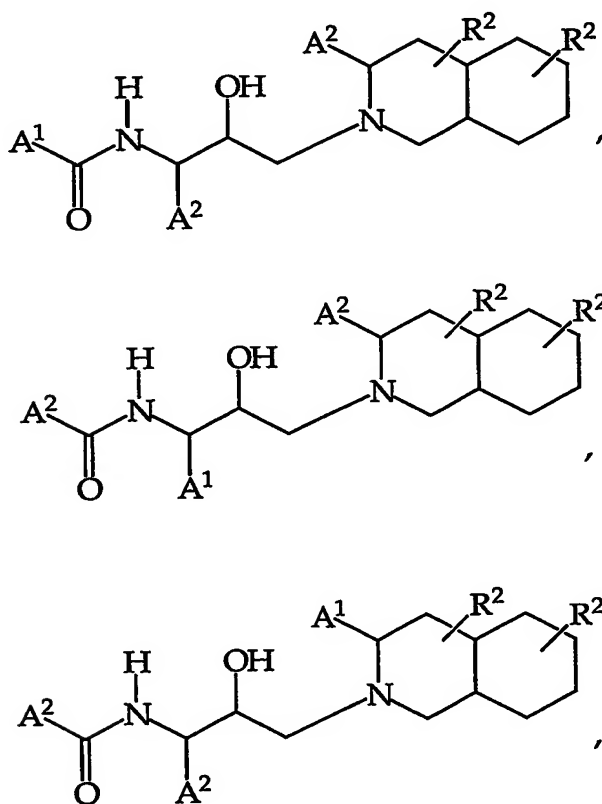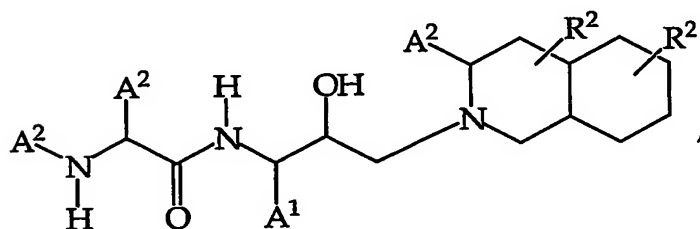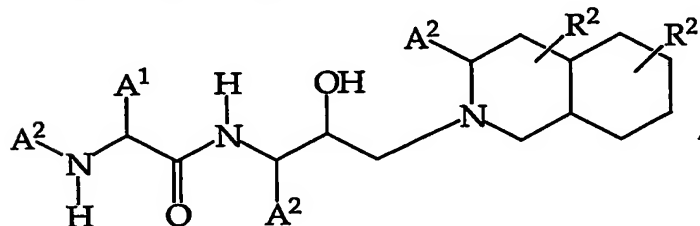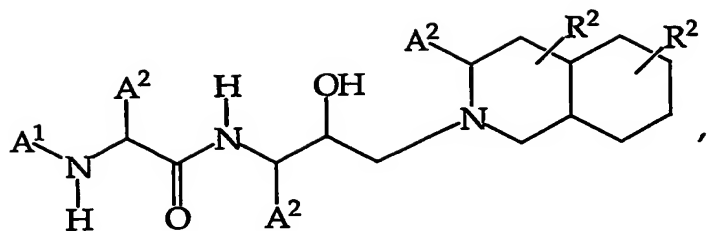
and
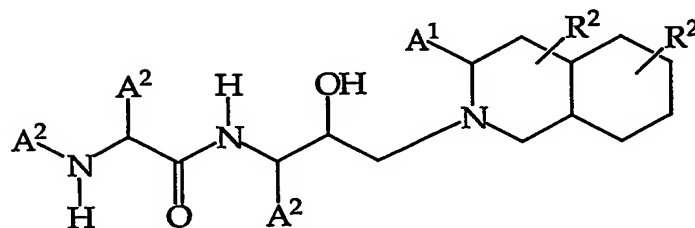
160.   The improved HIV protease inhibitor compound of claim 154 of the Formulas:

, ,

and

and
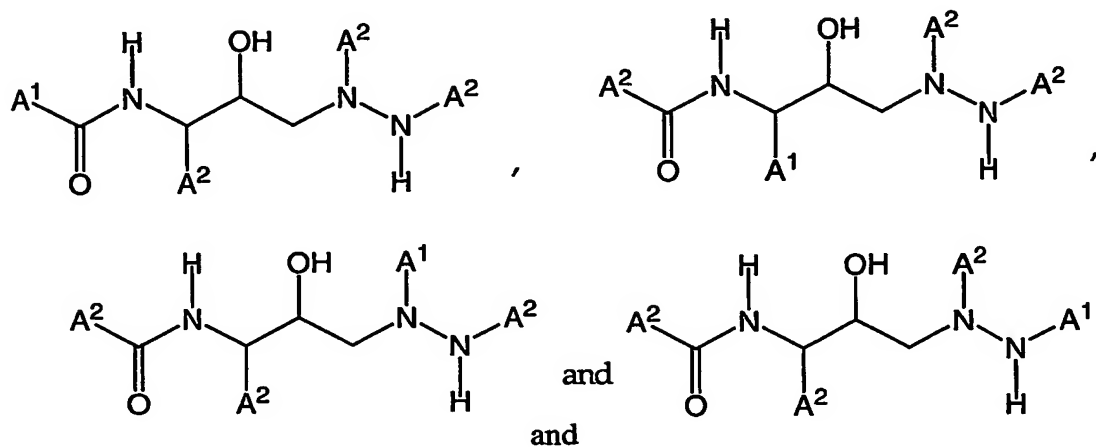
5

161.   The improved HIV protease inhibitor compound of claim 154 of the Formulas:

and
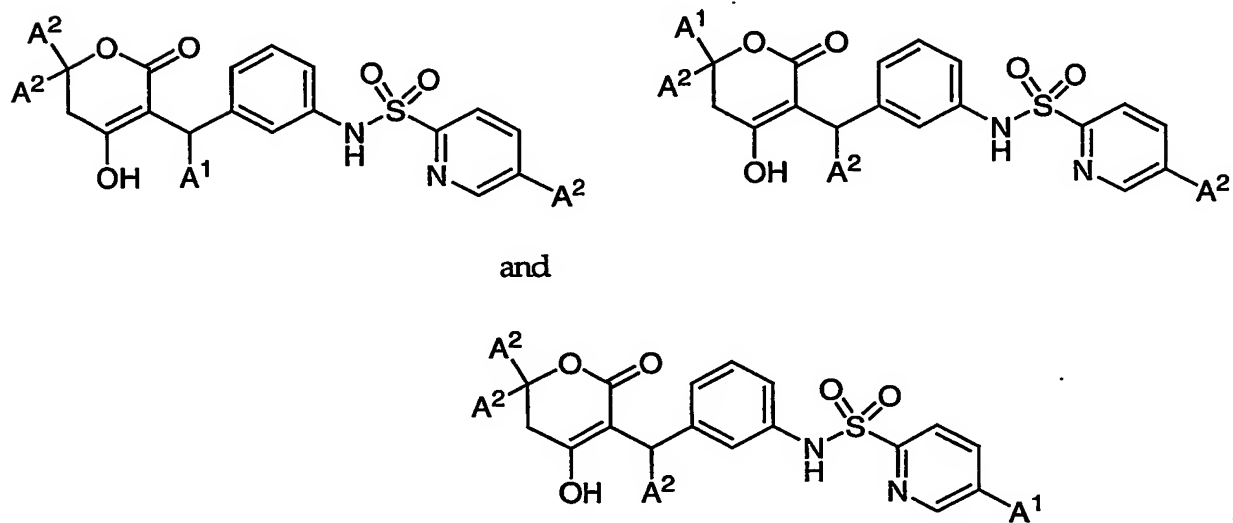
162.   The improved HIV protease inhibitor compound of claim 154 of the Formulas:

and
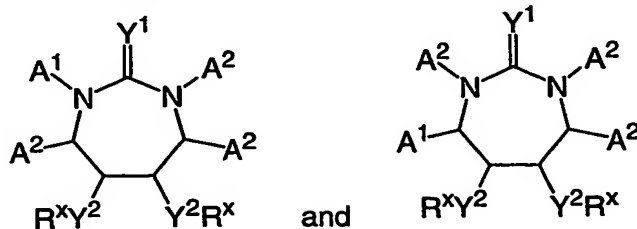
163.   The improved HIV protease inhibitor compound of claim 154 of the Formulas:

5

and
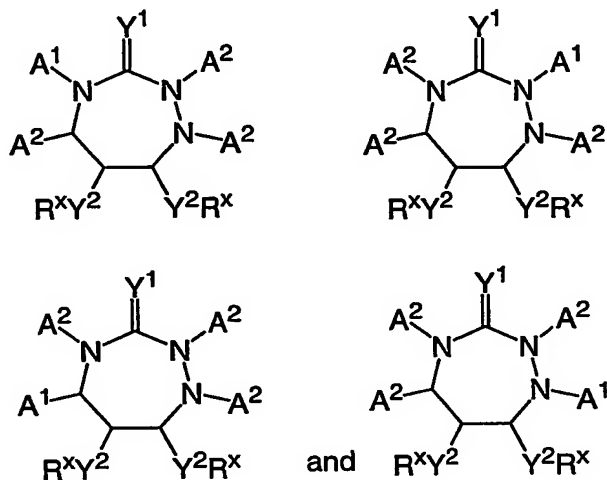
164.   The improved HIV protease inhibitor compound of claim 154 of the Formulas:

and
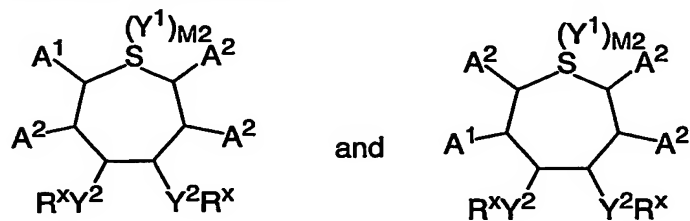
165.   The improved HIV protease inhibitor compound of claim 154 of the Formulas:

and
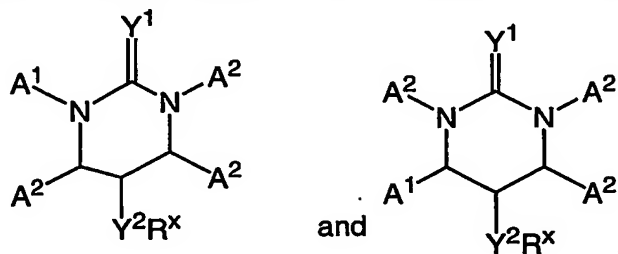
166. An MBF compound of Table 100.

167. A compound described herein.

5   168. A compound of Claim 167 described in the schemes or examples.

169. A method of making a compound described herein.

170. A method of Claim 169 described in the schemes or examples.

10

171. The use of a compound described here for treatment of HIV in humans.

172. The method of Claim 171 wherein the compound is described in the schemes or examples.

15

173   The use of a compound described here in the manufacture of a medicament.

174. The use of Claim 173 wherein the compound is described in the schemes or examples.

20

175. An HIV protease inhibitor compound capable of accumulating in human PBMCs.

176. The compound of Claim 175 further comprising a phosponate or phosphonate

25   prodrug.

177. The compound of Claim 176 wherein the phosphonate or phosphonate prodrug are of the formula A^3:

30   A^3 is:

Y^1 is independently O, S, $N(R^x)$, $N(O)(R^x)$, $N(OR^x)$, $N(O)(OR^x)$, or $N(N(R^x)(R^x))$;

Y^2 is independently a bond, O, $N(R^x)$, $N(O)(R^x)$, $N(OR^x)$, $N(O)(OR^x)$, $N(N(R^x)(R^x))$, $-S(O)_{M2}-$, or $-S(O)_{M2}-S(O)_{M2}-$;

R^x is independently H, R^1, W^3, a protecting group, or the formula:

R^y is independently H, W^3, R^2 or a protecting group;

R^1 is independently H or an alkyl of 1 to 18 carbon atoms;

R^2 is independently H, R^1, R^3 or R^4 wherein each R^4 is independently substituted with 0 to 3 R^3 groups;

R^3 is R^{3a}, R^{3b}, R^{3c} or R^{3d}, provided that when R^3 is bound to a heteroatom, then R^3 is R^{3c} or R^{3d};

R^{3a} is F, Cl, Br, I, -CN, N_3 or $-NO_2$;

R^{3b} is Y^1;

R^{3c} is $-R^x$, $-N(R^x)(R^x)$, $-SR^x$, $-S(O)R^x$, $-S(O)_2R^x$, $-S(O)(OR^x)$, $-S(O)_2(OR^x)$, $-OC(Y^1)R^x$, $-OC(Y^1)OR^x$, $-OC(Y^1)(N(R^x)(R^x))$, $-SC(Y^1)R^x$, $-SC(Y^1)OR^x$, $-SC(Y^1)(N(R^x)(R^x))$, $-N(R^x)C(Y^1)R^x$, $-N(R^x)C(Y^1)OR^x$, or $-N(R^x)C(Y^1)(N(R^x)(R^x))$;

R^{3d} is $-C(Y^1)R^x$, $-C(Y^1)OR^x$ or $-C(Y^1)(N(R^x)(R^x))$;

R^4 is an alkyl of 1 to 18 carbon atoms, alkenyl of 2 to 18 carbon atoms, or alkynyl of 2 to 18 carbon atoms;

R^5 is R^4 wherein each R^4 is substituted with 0 to 3 R^3 groups;

W^3 is W^4 or W^5;

W^4 is R^5, $-C(Y^1)R^5$, $-C(Y^1)W^5$, $-SO_2R^5$, or $-SO_2W^5$;

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W^5 is carbocycle or heterocycle wherein W^5 is independently substituted with 0 to 3 R^2 groups;

M2 is 0, 1 or 2;

M12a is 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11 or 12;

M12b is 0, 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11 or 12;

M1a, M1c, and M1d are independently 0 or 1; and

M12c is 0, 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11 or 12.

178.   The compound of Claim 177 wherein the intracellular half-life of the compound or an intracellular metabolite of the compound in human PBMCs is improved when compared to an analog of the compound not having the phosphonate or phosphonate prodrug.

179.   The compound of Claim 178 wherein the half-life is improved by at least about 50%.

180.   The compound of Claim 178 wherein the half-life is improved by at least about 100%.

181.   The compound of Claim 178 wherein the intracellular half-life of a metabolite of the compound in human PBMCs is improved when compared to an analog of the compound not having the phosphonate or phosphonate prodrug.

182.   The compound of Claim 181 wherein the half-life is improved by at least about 50%.

183.   The compound of Claim 181 wherein the half-life is improved by at least about 100%.

184.   The compound of Claim 181 wherein the half-life is improved by greater than 100%.

185. Use of a compound of the invention for the treatment of HIV infection.

186. Use of a compound of the invention in the manufacture of a medicament.

187. Use of a compound of the invention in the manufacture of a medicament
5   for the treatment of disorders affecting white blood cells.

188. Method of treating a disorder affecting white blood cells, comprising:
administering a compound of the invention to a patient in need of white-
blood-cell targeting.
10

189. Method of targeting a compound to white blood cells, comprising:
selecting a compound having a desired pharmaceutical activity and having a
first structure;
modifying said first structure by replacing one or more atom of said first structure
15   with an organic substituent comprising a phosphonate group or incipient
phosphonate group to provide a compound having a second structure.

190. A method of manufacturing a non-nucleoside compound having both
selectivity for white blood cells and a desired pharmaceutical activity, comprising:
20   chemically synthesizing a first molecule having a first structure containing a
phosphonate or incipient phosphonate group, wherein said first structure differs
from a second structure of a compound known to have said desired pharmaceutical
activity by having at least one hydrogen atom of said second structure replaced by
an organic substituent comprising a phosphonate group or incipient phosphonate
25   group.

191. The method of claim 190, wherein said first molecule is synthesized by a
series of chemical reactions in which a hydrogen of said second structure is replaced
by said organic substituent.
30

192. The method of claim 190, wherein said first molecule is synthesized by a
series of chemical reactions that never includes a molecule of said second structure.

193. Method of accumulating an HIV protease inhibitor inside a white blood
35   cell, comprising:
administering to a sample a composition comprising a compound of the
invention.

194.   The method of Claim 193 wherein said sample is a patient.
40

195. The method of claim 193, wherein said compound of the invention has a
chemical structure A-B, wherein (a) a compound having structure A-H has HIV
protease inhibitor activity and (b) substructure B comprises a phosphonate group or
incipient phosphonate group.
45

196. Method of increasing half-life of a non-nucleoside compound having anti-retroviral activity, comprising:

replacing at least one hydrogen atom or organic radical of said compound by an organic substituent comprising a phosphonate group or incipient phosphonate.

5

197. Method of designing a drug having specificity for white blood cells for synthesis, comprising:

obtaining a first list of first compounds having a desired activity;

5   creating a second list of second compounds, each of said second compounds having a structure in which at least one hydrogen atom or organic radical of a compound of said first list has been replaced by an organic substituent comprising a phosphonate group or incipient phosphonate group; and

selecting a synthetic pathway capable of producing some or all of said second
10   compounds from available starting materials, thereby providing a third list of compounds and associated synthetic techniques.

198. Method of manufacturing a pharmaceutical composition having said specificity of claim 197, comprising:

15   synthesizing a compound selected from said third list using said associated synthetic technique; and

admixing said synthesized compound with a pharmaceutically acceptable carrier.

20   199. A composition produced by the method of claim 198.

200. Method for producing a pharmaceutical composition having specificity for white blood cells, comprising:

admixing a therapeutically effective amount of a compound of the invention
25   with a pharmaceutically acceptable carrier.

30